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PHYTOCHEMICAL CONSTITUENT'S ANALYSIS AND CARDIO PROTECTIVE AGENT MECHANISM OF ALLIUM SATIVUM: A PHARMACOGENETIC APPROACH TO GARLIC DERIVED ORGANOSULFUR COMPOUND

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Abstract

Allium sativum L., commonly known as garlic, has occupied a prominent position in both traditional medicine and modern pharmacological research owing to its multifaceted therapeutic potential. Beyond its culinary use, garlic is widely recognized as a rich reservoir of bioactive phytochemicals, particularly organosulfur compounds, which contribute to its broad spectrum of biological activities. The present study attempts to analyze the diverse phytochemical constituents of A. sativum and to elucidate its cardio protective mechanism through a pharmacogenetic perspective. Special emphasis is placed on the chemical nature, biosynthetic pathways, and biological significance of major sulfur-containing compounds such as allicin, alliin, S-allyl cysteine, and ajoene.Cardiovascular diseases (CVDs) continue to be the leading cause of morbidity and mortality worldwide, primarily due to oxidative stress, dyslipidemia, hypertension, and endothelial dysfunction. Garlic-derived organosulfur compounds exhibit remarkable cardio protective actions by modulating lipid metabolism, reducing oxidative damage, inhibiting platelet aggregation, and improving vascular elasticity.

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Introduction

Garlic (Allium sativum L.), belonging to the family Amaryllidaceae, has been one of the most valuable medicinal plants used since ancient civilizations including the Egyptians, Greeks, Romans, Chinese, and Indians. Its extensive application in both traditional and modern medicine is attributed to its remarkable spectrum of biological activities. Garlic has been recognized not only as a flavoring agent in culinary practices but also as a natural therapeutic source possessing antimicrobial, antioxidant, antihypertensive, antithrombotic, and cardio protective properties.The pharmacological importance of garlic mainly arises from its rich phytochemical composition, particularly its organosulfur compounds (OSCs), flavonoids, saponins, and phenolic constituents. The characteristic pungent odor and potent medicinal efficacy of garlic are linked to sulfur-containing compounds such as allicin, alliin, ajoene, diallyl disulfide (DADS), diallyl trisulfide (DATS), and S-allyl cysteine (SAC). Among these, allicin is the principal bioactive compound formed when garlic cloves are crushed or chopped, activating the enzyme alliinase, which converts alliin to allicin [1]. However, allicin is highly unstable and rapidly decomposes into other biologically active derivatives that contribute to garlic's wide-ranging therapeutic profile. From a pharmacogenetic standpoint, garlic serves as a classical example of how natural products bridge traditional healing systems with evidence-based pharmacological research. The phytochemical constituents are responsible for regulating several biochemical pathways that mitigate cardiovascular risk factors. They act by reducing lipid peroxidation, inhibiting platelet aggregation, lowering serum cholesterol, and modulating nitric oxide synthesis, which collectively main-

tain vascular homeostasis and enhance myocardial function.

Additionally, oxidative stress and inflammation are major contributors to the progression of cardiovascular diseases (CVDs). Garlic-derived compounds function as potent antioxidants, scavenging free radicals and protecting myocardial cells from oxidative damage. They also upregulate endogenous antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT), thereby strengthening the cellular defense mechanisms.Moreover, epidemiological studies have suggested that regular dietary intake of garlic significantly correlates with a reduced incidence of atherosclerosis, hypertension, and coronary artery disease (CAD). The pharmacognostic approach toward garlic thus encompasses both morphological and phytochemical characterization, ensuring the standardization and quality control of garlic-based formulations used in herbal and clinical [2].

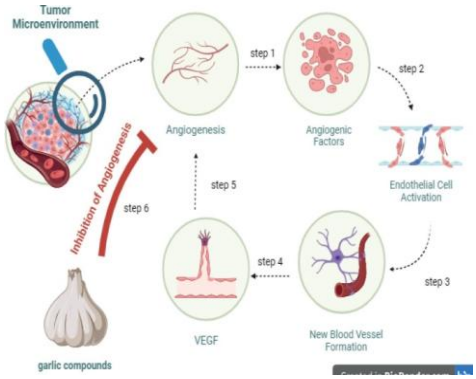

Fig 01: Angiogenesis processes and garlic compound interference

Phytochemical Constituent's Analysis

Allium sativum (garlic) is a vital medicinal herb rich in diverse bioactive phytochemicals responsible for its wide pharmacological actions. The major constituents include organosulfur compounds, flavonoids, saponins, and phenolic acids, each contributing uniquely to its therapeutic potential. Among the sulfur-based components, allicin, alliin, ajoene, diallyl disulfide (DADS), and S-allyl cysteine (SAC) are the primary bioactive molecules. These compounds are generated through enzymatic conversion when garlic is crushed, initiating the transformation of alliin to allicin by the enzyme alliinase.The organosulfur compounds are known to exhibit potent antioxidant properties, effectively scavenging reactive oxygen species (ROS) and enhancing cellular defense mechanisms. Furthermore, flavonoids such as quercetin, kaempferol, and apigenin present in garlic contribute to anti-inflammatory and lipid-regulating effects. Studies have shown that ethanol and aqueous extracts of garlic bulbs demonstrate significant in vitro free radical scavenging activity comparable to synthetic antioxidants like BHT and ascorbic acid (Singh et al., 2020). Phytochemical Constituents Analysis and Cardio protective Mechanism of Allium sativum (Garlic) [3]. Allium sativum (garlic) is a vital medicinal herb rich in diverse bioactive phytochemicals responsible for its wide pharmacological actions. The major constituents include organosulfur compounds, flavonoids, saponins, and phenolic acids, each contributing uniquely to its therapeutic potential. Among the sulfur-based components, allicin, alliin, ajoene, diallyl disulfide (DADS), and S-allyl cysteine (SAC) are the primary bioactive molecules. These compounds are generated through enzymatic conversion when garlic is crushed, initiating the transformation of alliin to allicin by the enzyme alliinase.

The phytochemical screening of Allium sativum typically involves methods such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography–Mass Spectrometry (GC-MS), and Fourier Transform Infrared Spectroscopy (FTIR). These techniques confirm the presence of key metabolites responsible for its cardio protective effects. The HPLC fingerprinting reveals dominant peaks corresponding to allicin and SAC, confirming their stability in aqueous extracts, whereas GC-MS profiling identifies volatile sulfur compounds that contribute to both aroma and pharmacological activity.Moreover, secondary metabolites like steroidal saponins and terpenoids synergize with sulfur constituents, enhancing anti-atherosclerotic and hypolipidemic effects. The cumulative presence of these phytochemicals supports garlic's role as a functional food and natural cardio protective agent [4].

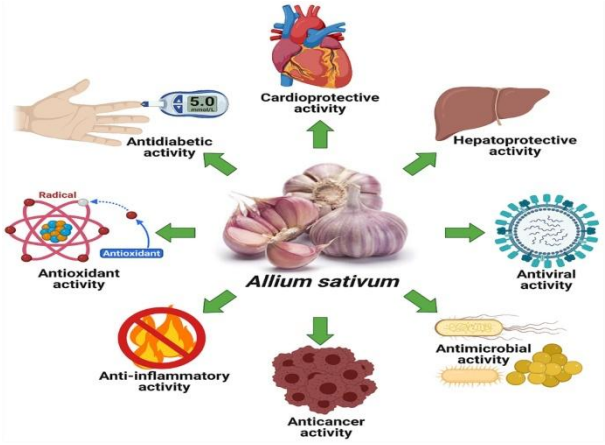

Fig 02: Pharmacological activities of garlic (Allium sativum)" or "Health benefits of garlic.".

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Garlics Cardio Protective Mechanism

Garlic's cardio protective mechanism is multifactorial. Beyond lipid modulation, it involves suppression of angiotensin-converting enzyme (ACE) activity, thereby control-

ling hypertension. Additionally, S-allyl cysteine has been reported to reduce myocardial damage by preventing calcium overload and stabilizing mitochondrial membranes. Through the activation of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, garlic enhances endogenous defense systems within cardiac tissues. Several in vivo and in vitro studies confirm that continuous garlic supplementation improves cardiac function, reduces serum triglycerides, and prevents cardiac hypertrophy. The pharmacognostic approach ensures that these effects are scientifically validated through both morphological and biochemical analyses of the plant. This integration of traditional knowledge with modern pharmacology reaffirms garlic's role as a natural cardio protective agent with broad therapeutic relevance.

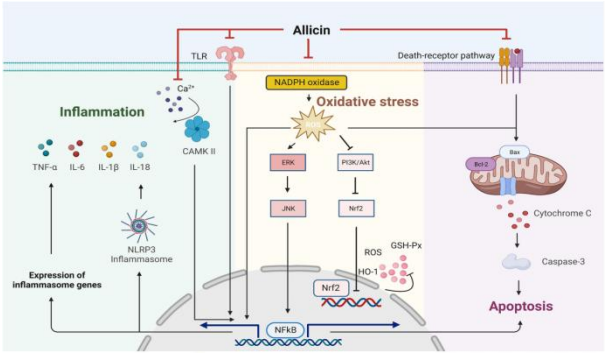

Fig 03: Molecular Mechanism of Garlic as a Cardio protective Agent

Garlic's cardio protective mechanism operates through multiple biochemical and molecular pathways, primarily driven by its organosulfur compounds (OSCs) such as allicin, diallyl disulfide (DADS), S-allyl cysteine (SAC), and ajoene. These bioactive molecules collectively regulate lipid metabolism, oxidative stress, endothelial function, and myocardial integrity [6].

1. **Antioxidant and Free Radical Scavenging Pathway** Oxidative stress plays a central role in the initiation of atherosclerosis and cardiac tissue injury. Garlic-derived compounds directly scavenge reactive oxygen species (ROS) and reactive nitrogen species (RNS), reducing lipid peroxidation in cardiac cells.S-allyl cysteine (SAC) increases the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx).This enhancement of the antioxidant defense system protects the myocardium from ischemia-reperfusion injury.Allicin inhibits the formation of malondialdehyde (MDA), a marker of oxidative lipid damage, thereby improving membrane stability of cardiomyocytes.
2. **Anti-hyperlipidemic and Anti-atherosclerotic Effects** Garlic helps maintain plasma lipid homeostasis by influencing hepatic enzymes involved in cholesterol biosynthesis.It suppresses HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis, similar to statins [7]. Organosulfur compounds enhance cholesterol catabolism and excretion through bile acids. Studies reveal that regular garlic intake significantly decreases total cholesterol, LDL, and triglycerides, while elevating HDL cholesterol, thus preventing the deposition of fatty plaques in arteries. This effect directly reduces the risk of coronary artery disease (CAD) and atherosclerosis.

Clinical Investigations and Pharmacological Validation of Garlic's Cardio Protective Efficacy

The cardio protective potential of Allium sativum has been extensively validated through a combination of clinical trials, animal experiments, and biochemical investigations, offering strong pharmacological evidence for its use as a natural therapeutic agent. These studies emphasize the role of garlic-derived organosulfur compounds (OSCs) in improving cardiovascular performance, lipid regulation, and endothelial protection.

Clinical studies involving hypercholesterolemia and hypertensive patients have demonstrated that daily consumption of aged garlic extract (AGE) or powdered garlic tablets leads to a measurable decline in total serum cholesterol, LDL cholesterol, and triglycerides, accompanied by a significant increase in HDL cholesterol. In a double-blind, placebo-controlled trial conducted by Bordia et al. (1998), subjects who consumed garlic extract for 12 weeks showed a 12–15% reduction in LDL cholesterol and a 10% improvement in HDL levels, thereby affirming its anti-atherosclerotic activity [8]. Further, a clinical evaluation by Ried et al. (2016) confirmed garlic's ability to modulate blood pressure. The study revealed that aged garlic extract significantly reduced both systolic and diastolic pressure in patients with uncontrolled hypertension, with an average drop of 8–10 mmHg. This antihypertensive action is primarily attributed to enhanced nitric oxide (NO) synthesis and improved endothelial function, which together facilitate arterial relaxation and blood flow regulation. Experimental models using Wistar rats and albino mice have provided deeper mechanistic insight. In isoproterenol-induced myocardial infarction models, administration of garlic extract significantly reduced levels of serum creatine kinase (CK-MB), lactate dehydrogenase (LDH), and troponin-T, indicating strong myocardial protection. Histopathological examinations revealed decreased necrosis and better preservation of cardiac muscle architecture, which supports the anti-apoptotic and membrane-stabilizing properties of garlic's organosulfur compounds.

Garlic's hypolipidemic and antioxidative properties also contribute to its clinical significance. In diabetic and obese patients, garlic supplementation has been shown to reduce oxidative biomarkers such as malondialdehyde (MDA) and increase antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx). These biochemical changes are closely linked to improved cardiac function and prevention of vascular complications. Standardization is crucial because the biological activity of Allium sativum is largely dependent on its allicin yield, which can

vary due to factors like drying, temperature, and extraction methods [9].

Experimental Pharmacology and Comparative Analysis of Garlic Extracts

Pharmacological investigations of Allium sativum have extensively demonstrated its efficacy as a cardio protective , antihyperlipidemic, antihypertensive, and antioxidant agent. These experimental studies have been carried out using both in vivo and in vitro models to evaluate the bioactivity of garlic-derived organosulfur compounds under controlled laboratory conditions. The in vivo models, primarily involving Wistar rats, albino mice, and rabbits, have provided strong evidence regarding the therapeutic potential of garlic. When administered to animals subjected to isoproterenol- or doxorubicin-induced myocardial infarction, garlic extracts significantly reduced serum biomarkers of cardiac injury such as creatine kinase-MB (CK-MB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH). These biochemical findings correlated with histopathological studies that showed decreased necrosis, reduced enema, and preservation of myocardial Fiber integrity [10]. In oxidative stress models, methanolic extracts of garlic enhanced the levels of superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase, while lowering malondialdehyde (MDA) and nitrite concentrations. This biochemical modulation confirms the antioxidant and cytoprotective roles of garlic's Sulphur compounds; particularly S-allyl cysteine (SAC) and allicin. A comparison of various extraction methods has revealed marked differences in the yield and potency of active compounds. Aged garlic extract (AGE), prepared by storing fresh garlic in ethanol for extended periods, exhibits superior stability and reduced toxicity compared to raw or oil-based extracts. This aging process leads to the conversion of unstable allicin into more stable and bioavailable compounds such as S-allyl cysteine (SAC) and S-allyl mercaptocysteine (SAMC), which show enhanced pharmacokinetic profiles. In contrast, aqueous and ethanolic extracts contain higher concentrations of polar flavonoids and phenolic compounds, contributing to their strong antioxidant capacity. Studies comparing methanolic, aqueous, and ethyl acetate extracts have shown that the methanolic fraction possesses the highest radical scavenging activity, followed by ethanolic and aqueous extracts. The superior efficacy of methanol is attributed to its ability to dissolve a broader range of phenolic and sulfur-based constituents [11].

In vitro assays further confirm garlic's pharmacological properties. Techniques like DPPH free radical scavenging, ferric reducing antioxidant power (FRAP), and nitric oxide inhibition assays have consistently demonstrated that garlic extracts significantly enhance antioxidant potential and protect endothelial cells against oxidative injury. The lipid peroxidation assay revealed that garlic extract prevents the oxidation of low-density lipoproteins (LDL), a key step in the initiation of atherosclerosis.Moreover, garlic's ACE (angiotensin-converting enzyme) inhibitory activity has been evaluated using biochemical and computational models. The organosulfur compound ajoene was found to bind effectively with the active site of ACE, thereby inhibiting the conversion of angiotensin I to angiotensin II. This mechanism elucidates garlic's vasodilatory and antihypertensive effects.

Comparative pharmacological evaluations also indicate synergistic interactions between organosulfur compounds and flavonoids present in garlic. This synergism enhances the compound's bioefficacy, offering multidimensional protection to the cardiovascular system. The cumulative evidence suggests that the therapeutic value of garlic is determined not by a single molecule, but by the integrated activity of its complex phytochemical network.

Toxicological evaluation and safety profile of garlic extractsal though Allium sativum is widely regarded as one of the safest herbal agents, its pharmacological potency demands a careful evaluation of toxicological parameters. The safety of garlic-derived compounds depends on the dosage, formulation type, and duration of consumption. Hence, toxicological studies play a crucial role in establishing the therapeutic index and determining the threshold of bioactive compound tolerance.Experimental studies conducted on rodent and rabbit models have confirmed that garlic extracts exhibit an excellent safety profile when administered at therapeutic doses. The LD_{50} (lethal dose for 50% of animals) of aqueous garlic extract was found to be greater than 2000 mg/kg, indicating low acute toxicity [12]. Chronic administration of aged garlic extract (AGE) for 90 days revealed no significant alterations in hepatic, renal, or hematological parameters. Liver enzyme levels such as ALT, AST, ALP, and bilirubin remained within the normal range, confirming that garlic does not induce hepatocellular injury at pharmacologically relevant doses. However, certain mild side effects, including gastrointestinal discomfort, allergic reactions, and odor-related intolerance, have been reported, particularly with raw or oil-based garlic preparations. These adverse effects are usually transient and dose-dependent. High intake of raw garlic (more than 5 g/day) can cause gastric irritation, flatulence, or heartburn, primarily due to the presence of sulfur-rich volatile compounds like diallyl disulfide and allyl mercaptan. The haematological safety profile of garlic has been extensively studied. Results show no significant changes in total RBC, WBC, or platelet counts after prolonged administration. On the contrary, some studies indicate that garlic may enhance platelet elasticity and reduce blood viscosity, which could indirectly support its cardio protective role. Toxicity assessments involving histopathological examination of liver, kidney, and heart tissues also revealed no pathological lesions, fibrosis, or necrotic damage, further affirming its biocompatibility. Interestingly, garlic's antioxidant potential counteracts oxidative stress-induced hepatotoxicity and nephrotoxicity caused by other drugs, such as aceta-

minophen and gentamicin. This protective role emphasizes garlic's potential as both a therapeutic and detoxifying agent. At the molecular level, garlic's sulfur compounds influence detoxification enzymes in the liver. Compounds like S-allyl cysteine and diallyl disulfide modulate phase II detoxification enzymes, including glutathione S-transferase (GST) and quinone reductase (QR), which play vital roles in neutralizing reactive metabolites. This mechanism supports garlic's chemo-preventive and hepatoprotective properties [13].

Table 01: Toxicological Parameters Observed in Animal Studies

Parameter	Observation	Reference Range	Remark
Alt/Ast	Normal	20–45 U/L	No Hepatic Toxicity
Urea/Creatinine	Normal	0.5–1.2 Mg/Dl	No Renal Toxicity
Rbc/Wbc Count	Normal	Stable	Haematological Function [14]

Extraction and Isolation of Photochemical Constituents

1. **Extraction Techniques of Organosulfur Compounds**: The phytochemical analysis of Allium sativum involves careful extraction of its bioactive constituents to preserve their chemical stability and therapeutic potency. Common extraction methods include aqueous maceration, ethanolic extraction, steam distillation, and supercritical CO_2 extraction. Among these, steam distillation is particularly effective in isolating volatile sulfur compounds such as allicin, ajoene, diallyl sulfide (DAS), and diallyl disulfide (DADS).Aqueous extraction primarily yields hydrophilic antioxidants, amino acids, and flavonoids. Organic solvent extraction (ethanol, methanol, chloroform) enhances recovery of organosulfur derivatives and lipid-soluble components. Supercritical CO_2 extraction provides high-purity fractions with minimal degradation, preserving thermolabile compounds like S-allyl cysteine (SAC).
2. **Isolation and Characterization:** After extraction, the identification and isolation of phytochemicals are carried out through chromatographic and spectroscopic techniques: Thin Layer Chromatography (TLC) and High-Performance Liquid Chromatography (HPLC) help separate thiosulfinates and allyl sulfides.Gas Chromatography-Mass Spectrometry (GC-MS) provides molecular fingerprints for volatile compounds such as allicin and allyl methyl sulfide.Nuclear Magnetic Resonance (NMR) spectroscopy elucidates structural features of garlic-derived organosulfur molecules.15These techniques collectively enable quantitative and qualitative evaluation of the bioactive constituents responsible for garlic's cardio protective activities.
3. **Standardization and Quality Control:** Standardization ensures that Allium sativum preparations maintain consistent potency and safety. The concentration of allicin serves as a key marker compound for assessing pharmacological quality.
4. **Parameters Evaluated Include:** Moisture content and ash values (to assess purity)Sulfur content analysis (for metabolic activity prediction). pH, extractive values, and chromatographic profiles. Through these measures, both raw garlic and commercial formulations (like aged garlic extract and garlic oil) are standardized for therapeutic use.

Mechanistic insights into the cardio protective role of garlic organosulfur compounds: The cardio protective mechanism of Allium sativum is a multifaceted biochemical process involving modulation of lipid metabolism, enhancement of antioxidant defense, and inhibition of platelet aggregation. The major active principles-allicin, ajoene, S-allyl cysteine (SAC), and diallyl disulfide (DADS)-interact with critical molecular targets within cardiovascular tissues to maintain myocardial integrity and vascular health.

1. **Modulation of Lipid Metabolism:** Garlic-derived organosulfur compounds exert hypolipidemic effects by regulating hepatic enzymes involved in cholesterol biosynthesis, particularly 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Inhibition of this enzyme leads to reduced endogenous cholesterol synthesis, subsequently decreasing serum low-density lipoprotein (LDL) and triglyceride levels. Simultaneously, there is an elevation in high-density lipoprotein (HDL) concentration, promoting reverse cholesterol transport and preventing lipid accumulation in arterial walls [16].
2. **Enhancement of Endogenous Antioxidant Defense**: The reactive oxygen species (ROS) generated during oxidative stress play a pivotal role in the pathogenesis of myocardial injury. Garlic constituents, particularly SAC and DADS, activate nuclear factor erythroid 2–related factor 2 (Nrf2) signaling pathways. This transcriptional activation enhances the expression of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT). Consequently, lipid peroxidation is reduced, and cardiac tissue experiences decreased oxidative damage.
3. **Anti-Inflammatory and Anti-Atherogenic Pathways:** Garlic bioactives modulate pro-inflammatory cytokines like TNF-α, IL-6, and CRP, which are crucial mediators in atherosclerosis progression. The inhibition of NF-κBsignaling prevents the transcription of inflammatory genes, attenuating vascular inflammation and endothelial dysfunction [17]. Moreover, ajoene inhibits platelet aggregation by altering

thromboxane A_2 synthesis, thereby reducing thrombus formation and maintaining smooth blood flow dynamics.

4. **Modulation of Nitric Oxide (NO) and Vascular Tone:** Garlic extracts enhance the bioavailability of nitric oxide by stimulating endothelial nitric oxide synthase (eNOS) activity. This vasodilatory effect improves coronary blood circulation and decreases vascular resistance, leading to a reduction in hypertension-related cardiac strain. The synergistic interaction between SAC and allicin amplifies NO-mediated vascular relaxation, contributing to improved endothelial function.
5. **Protection against Myocardial Ischemia-Reperfusion Injury:** During ischemic events, the heart experiences oxygen deprivation, leading to mitochondrial dysfunction and calcium overload. Garlic compounds protect cardiac mitochondria by preserving membrane potential, inhibiting apoptosis-related pathways, and reducing cytochrome c release. SAC's antioxidant property stabilizes cardiomyocytes, preventing cell death during reperfusion [18].

Pharmacognostic and Analytical Evaluation of Organosulfur Compounds from Allium Sativum

The pharmacogenetic examination of Allium sativum emphasizes both macroscopic and microscopic parameters along with chemical profiling of its active organosulfur constituents. In the context of modern phytochemical research, the integration of chromatographic, spectroscopic, and bioassay-guided techniques has established a scientific foundation for the cardio protective efficacy of garlic extracts.

Macroscopic and Organoleptic Evaluation: Fresh bulbs of Allium sativum exhibit a characteristic pungent odor and spicy taste due to the enzymatic conversion of alliin into allicin. The cloves are white, oval, and covered by a papery tunic. The bulb contains multiple segments arranged concentrically, each representing a storage organ rich in volatile organosulfur oils [19].

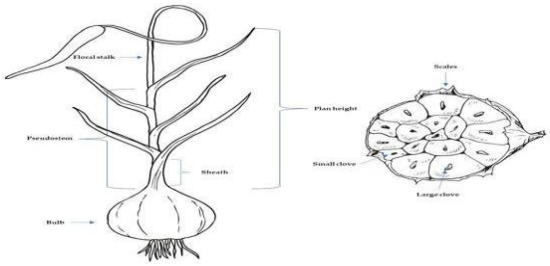

Fig 04: T.S (Transverse section) of garlic

Microscopic features and cellular characteristics: Transverse section of the garlic clove reveals parenchymatous cells, calcium oxalate crystals, and oil globules. Staining with Sudan III confirms the presence of lipid-based volatile oils. The cells exhibit numerous idioblasts containing precursor sulfur compounds. Under polarized light, vascular bundles show a reticulate arrangement typical of Liliaceae species [20].

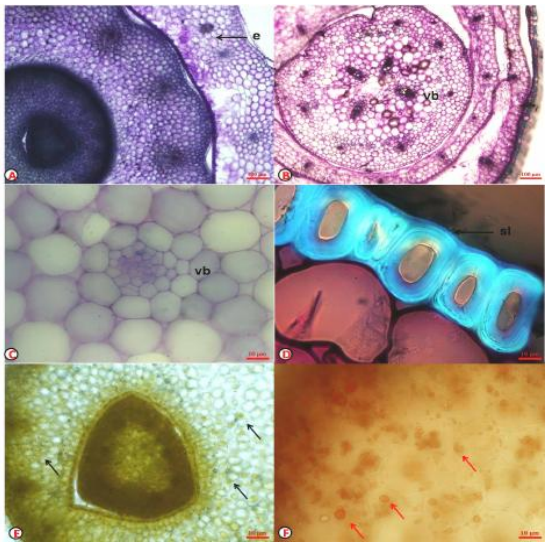

Fig 05: Microscopical Observation of garlic compound

Extraction and Isolation Procedures

The extraction of organosulfur compounds follows a sequential solvent extraction method using ethanol, methanol, and water. The freshly crushed bulbs are subjected to maceration or Soxhlet extraction. Allicin is produced in situ from alliin by the enzyme alliinase during crushing; hence fresh samples are preferred over dried ones.

1. Collection of Plant Material
2. Cleaning and Peeling Remove dirt, outer scales, and roots from garlic bulbs.
3. Drying Air dry or oven dry at low temperature (40–50°C) to remove moisture.
4. Size Reduction Grind or crush dried garlic cloves into fine powder.
5. Solvent Extraction Add powder to solvent (Ethanol/Methanol/Water).Keep mixture under shaking or reflux conditions.
6. Filtration Filter extract to remove solid residues.
7. Concentration Use rotary evaporator to remove solvent and obtain crude extract.
8. Fractionation (Optional) Separate extract into different fractions (hexane, chloroform, ethyl acetate, etc.) based on polarity [21].
9. Isolation of Bioactive Compounds Employ column chromatography or preparative TLC.
10. Purification and Characterization Identify and analyze isolated compounds using FTIR, HPLC, GC–MS, or NMR [22].

Anti-Inflammatory & Anti-Apoptotic Cascade

Garlic-Derived Organosulfur Compounds

↓

Inhibition of NF-κB Activation

↓

↓ Expression of TNF-α, IL-1β, IL-6

↓

Reduced Myocardial Inflammation
↓
↓ Oxidative Damage and Apoptosis

One of the central pathways involved in garlic's cardio protective mechanism is the PI3K/Akt signaling pathway. Activation of PI3K triggers phosphorylation of Akt, which in turn promotes cell survival, angiogenesis, and nitric oxide (NO) synthesis via stimulation of endothelial nitric oxide synthase (eNOS). Enhanced NO production causes vasodilation, reduces platelet aggregation, and improves myocardial perfusion [23]. Moreover, Akt signaling attenuates cardiac apoptosis by inhibiting the activation of caspase-3 and Bax, thereby preserving cardiomyocyte viability during ischemic stress [24].

Garlic's organosulfur compounds also play a key role in activating the Nrf2/ARE (nuclear factor erythroid 2–related factor 2 / antioxidant response element) pathway, which serves as a master regulator of the antioxidant defense system.25 Upon activation, Nrf2 dissociates from its cytoplasmic inhibitor Keap1 and translocates into the nucleus, where it binds to ARE sequences to induce the expression of antioxidant and phase II detoxifying enzymes such as glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase (CAT), and heme oxygenase-1 (HO-1). This enhances the detoxification of reactive oxygen species (ROS) and limits lipid peroxidation within myocardial cells, contributing to oxidative stress resistance [26].

Anti-Apoptotic and Gene Modulatory Effects of Garlic-Derived Compounds

The cardio protective potential of Allium sativum extends beyond its antioxidant and metabolic regulatory roles, encompassing genetic and molecular control over apoptosis and gene expression. Apoptosis, or programmed cell death, plays a pivotal role in the progression of myocardial infarction, ischemia-reperfusion injury, and heart failure. Garlic-derived organosulfur compounds, especially S-allyl cysteine (SAC) and diallyl disulfide (DADS), have been reported to modulate apoptotic signaling by maintaining the delicate balance between pro-apoptotic and anti-apoptotic gene expression [27]. At the cellular level, allicin and SAC suppress the expression of Bax (Bcl-2-associated X protein) and caspase-3, which are major mediators of apoptotic cell death, while simultaneously upregulating the expression of Bcl-2 (B-cell lymphoma 2)-a critical anti-apoptotic protein that stabilizes the mitochondrial membrane. This balance prevents cytochrome c release into the cytosol and thereby halts the activation of the caspase cascade. Such regulatory effects preserve cardiomyocyte structure and functions, reducing tissue necrosis and myocardial remodeling.28Overall, the anti-apoptotic and gene regulatory effects of garlic-derived organosulfur compounds provide a molecular foundation for its long-recognized cardio protective action. The integration of anti-inflammatory, antioxidant, and anti-apoptotic signaling results in synergistic cardio protection, highlighting [29].

Garlic's Potential AsGarlic (Allium Sativum)
↓
Organosulfur Compounds (Allicin, SAC, DADS)
↓
Regulation Of Gene Expression
↓
↑ Bcl-2 ↓ Bax, Caspase-3
↓
Inhibition Of Mitochondrial Apoptosis
↓
↓ Oxidative Stress | ↓ Inflammation | ↑ Cell Survival
↓
Cardiomyocyte Protection and Functional Recovery A Nutraceutical Intervention in Cardiovascular Disorders.

Role of Garlic in Ischemia-Reperfusion Injury and Myocardial Remodelling

Ischemia-reperfusion (I/R) injury remains one of the critical pathological processes leading to myocardial cell death and post-infarction remodeling. Restoration of blood flow after a period of ischemia paradoxically aggravates tissue injury through sudden oxygen re-entry, calcium overload, and excessive generation of reactive oxygen species (ROS). Garlic-derived organosulfur compounds provide remarkable cardioprotection in this context by attenuating oxidative stress, stabilizing mitochondrial integrity, and preserving myocardial contractile function.30The antioxidant defense stimulated by compounds such as allicin, S-allyl cysteine (SAC), and diallyl trisulfide (DATS) mitigates ROS-induced lipid peroxidation and prevents damage to cardiolipin within mitochondrial membranes. These compounds enhance endogenous enzymatic antioxidants including glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT), which collectively scavenge superoxide and hydrogen peroxide radicals during reperfusion [31]. The activation of the Nrf2/ARE pathway and subsequent induction of heme oxygenase-1 (HO-1) further contributes to the suppression of oxidative burst and cellular necrosis.Collectively, these findings establish Allium sativum as a comprehensive cardio protective Phyto therapeutic agent, capable of intervening at multiple stages of cardiac injury [32]. Its integrated network of antioxidant, anti-apoptotic, anti-inflammatory, and antifibrotic mechanisms underpins its therapeutic potential in both preventive and post-ischemic cardiovascular management [33].

Conclusion

Garlic (Allium sativum) remains one of the most extensively studied medicinal plants for its cardio protective potential, primarily attributed to its diverse organosulfur compounds such as allicin, S-allyl cysteine, diallyl disulfide, and ajoene. These bioactive molecules exhibit a multifaceted mechanism of action involving antioxidant defence enhancement, lipid-lowering activity, antithrombotic properties, and modulation of endothelial nitric oxide pathways. Collectively, these effects contribute to reduced

oxidative stress, improved vascular tone, and suppression of atherogenic processes. Pharmacogenetic and phytochemical analyses have further reinforced garlic's therapeutic significance, providing valuable insights into its structural, biochemical, and molecular composition. Thus, Allium sativum exemplifies a natural cardio protective agent that bridges traditional herbal wisdom with modern pharmacological validation. Continued research focusing on molecular pharmacodynamics, dosage optimization, and formulation stability will strengthen its clinical application in cardiovascular therapeutics.

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Conflict of Interest
Authors are declared that no Conflict of Interest

Informed Consent and Ethical Statement
Not Applicable

Author Contribution
All authors are contributed equally.

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