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RESEARCH ARTICLE

The Effects of Garlic (*Allium sativum* L.) and Allicin on Heart Rate: A Systematic Review and Meta-Analysis of Experimental and Clinical Studies

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SUMMARY

Garlic (Allium sativum L.) has long been recognized for its cardiovascular benefits, including antihypertensive, antihyperlipidemic, and antioxidant effects. However, evidence regarding its influence on heart rate (HR) remains inconsistent across studies. This systematic review and meta-analysis aimed to evaluate the effects of garlic, Allium sativum, or allicin administration on HR and to explore the underlying mechanisms contributing to HR modulation. A comprehensive literature search was conducted in the Scopus and PubMed databases following PRISMA guidelines. Studies published in English from 2010 onward were included if they investigated the effect of garlic or allicin on HR or elucidated mechanisms related to HR regulation. Data extraction was performed independently by two reviewers, and analysis was based on mean and standard deviation (SD). Out of 175 initially identified records, 19 studies met the inclusion criteria, and 13 were included in the meta-analysis. Most human studies reported a modest HR reduction following garlic supplementation, with a pooled mean difference of approximately –5.57 ± 10.36 beats per minute (bpm). Consistent trends were observed in animal models, showing an average HR decrease of –50.06 ± 21.25 bpm. Mechanistic studies revealed that garlic and allicin influence HR through modulation of ion channels (Nav1.5 and Cav1.2), regulation of HCN4 expression, and antioxidant and parasympathetic activation pathways. Garlic and its bioactive compound allicin demonstrate HR-lowering potential through electrophysiological and autonomic modulation. However, the extent of HR change depends on dosage, extract formulation, and baseline cardiovascular status. Further standardized clinical trials are warranted to define optimal formulations and dosing strategies for cardiovascular applications.

Keywords: *Allium sativum, allicin, heart rate, cardiovascular regulation, systematic review, meta-analysis.*

Sarımsağın (Allium sativum L.) ve Alisinin Kalp Atım Hızı Üzerindeki Etkileri: Deneysel ve Klinik Çalışmaların Sistematik Derlemesi ve Meta-Analizi

ÖZ

Sarımsak (Allium sativum L.), antihipertansif, antihiperlipidemik ve antioksidan etkiler dahil olmak üzere kardiyovasküler yararlarıyla uzun süredir bilinmektedir. Ancak, kalp atım hızı (HR) üzerindeki etkisine ilişkin kanıtlar çalışmalar arasında tutarsızlık göstermektedir. Bu sistematik derleme ve meta-analiz, sarımsak, Allium sativum veya allisin uygulamasının HR üzerindeki etkilerini değerlendirmeyi ve HR düzenlenmesine katkıda bulunan altta yatan mekanizmaları araştırmayı amaçlamıştır. PRISMA yönergelerine uygun olarak Scopus ve PubMed veri tabanlarında kapsamlı bir literatür taraması yapılmıştır. 2010 yılından itibaren İngilizce yayımlanan ve sarımsak veya allisinin HR üzerindeki etkisini ya da HR düzenlenmesine ilişkin mekanizmaları inceleyen çalışmalar dahil edilmiştir. Veriler iki araştırmacı tarafından bağımsız olarak çıkarılmış ve analizler ortalama ile standart sapma (SD) değerlerine dayanmıştır. Başlangıçta belirlenen 175 çalışmadan 19'u dahil edilme kriterlerini karşılamış ve 13'ü meta-analize alınmıştır. İnsan çalışmalarının çoğu, sarımsak takviyesi sonrasında ortalama –5,57 ± 10,36 atım/dk düzeyinde hafif bir HR azalması bildirmiştir. Hayvan modellerinde benzer şekilde, ortalama –50,06 ± 21,25 atım/dk düzeyinde HR düşüşü gözlenmiştir. Mekanistik çalışmalar, sarımsak ve allisinin HR'yi iyon kanalları (Nav1,5 ve Cav1,2), HCN4 gen ekspresyonu, antioksidan ve parasempatik aktivasyon yolları üzerinden modüle ettiğini ortaya koymuştur. Sarımsak ve biyoaktif bileşiği allisin, elektrofizyolojik ve otonom mekanizmalar aracılığıyla HR düşürücü potansiyele sahiptir. Ancak, bu etkinin derecesi doz, ekstre formülasyonu ve kardiyovasküler durum gibi faktörlere bağlıdır.

Anahtar Kelimeler: *Allium sativum, allisin, kalp atım hızı, kardiyovasküler düzenleme, sistematik derleme, meta-analiz.*

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INTRODUCTION

Garlic (*Allium sativum* L.) has long been recognized not only as a culinary ingredient that enhances the flavor of food but also as a medicinal plant with a broad spectrum of therapeutic activities (Ha et al., 2024). Throughout history, it has been utilized in various traditional medical systems for its beneficial effects on human health, particularly in the prevention and management of cardiovascular disorders. Modern pharmacological studies have confirmed that garlic exerts antihypertensive, antihyperlipidemic, antithrombotic, and antioxidant effects, as well as immunomodulatory properties. Garlic is characterized predominantly by organosulfur constituents, with intact cloves containing *S*-alk(en)yl-*L*-cysteine sulfoxides and related γ-glutamyl peptides. Upon tissue disruption, alliinase rapidly converts alliin to allicin (diallyl thiosulfinate), a reactive and transient compound that further yields secondary sulfur metabolites such as ajoene, vinyldithiins, and diallyl sulfides, alongside water-soluble derivatives (e.g., *S*-allyl cysteine) (Sasmaz et al., 2025). These sulfur-containing metabolites are pharmacologically significant and are widely linked to garlic's cardioprotective and vascular effects, inhibition of platelet aggregation, and antioxidant/anti-inflammatory as well as antimicrobial activities (Sleiman et al., 2024; Supa-aksorn et al., 2025).

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, and heart rate (HR) is considered a vital physiological parameter closely associated with cardiovascular outcomes. Elevated HR has been independently linked to increased risks of hypertension, atherosclerosis, and cardiac mortality. Therefore, identifying natural agents capable of modulating HR may contribute to the development of complementary strategies for cardiovascular protection (Bernal-Sánchez et al., 2026; Mahfoud et al., 2024).

Interestingly, the relationship between garlic administration and HR regulation remains controversial. Some experimental and clinical studies have reported that garlic or allicin supplementation can lower HR through mechanisms involving vasodilation, enhanced parasympathetic activity, and reduced oxidative stress (Asdaq & Inamdar, 2011; Brankovic et al., 2011; Khastkhodaei et al., 2011). Conversely, other studies have shown either an increase or no significant change in HR, with variations attributed to differences in dosage, formulation, duration of administration, and experimental models used. These inconsistencies indicate that the effects of garlic on HR, as well as the underlying mechanisms, are not yet fully elucidated.

Given the growing interest in herbal-based cardiovascular therapies and the inconsistent findings across studies, a systematic review and meta-analysis are warranted to synthesize current evidence. This study therefore aims to identify changes in HR following administration of garlic, *A. sativum*, or allicin, in different formulations, including whole garlic preparations and standardized extracts, as well as isolated bioactive compounds such as allicin, and provide an integrated understanding of the mechanisms by which garlic influences HR regulation. By quantitatively synthesizing HR outcomes and integrating mechanistic evidence, this study addresses inconsistencies in the existing literature and provides a focused evaluation of formulation- and dose-dependent effects that have not been systematically examined in previous reviews. The findings are expected to clarify the cardiovascular role of garlic and strengthen the scientific foundation for its application as an evidence-based herbal intervention in modern medicine.

MATERIALS AND METHODS

Search strategy and study selection

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two independent researchers evaluated all retrieved manuscripts to ensure accuracy and minimize selection bias.

A comprehensive literature search was performed in two electronic databases, Scopus and PubMed, to identify relevant publications addressing both research objectives. The search strategy employed four sets of keywords, including both Medical Subject Headings (MeSH) and All Field terms.

For the first objective (to identify changes in heart rate following *garlic/Allium sativum/allicin* administration), the search strings applied were "((garlic [MeSH Terms]) OR (allium [MeSH Terms])) AND (heart rate [MeSH Terms])" for MeSH Terms, and "((“garlic”) OR (“allium”) OR (“allicin”)) AND (“heart rate”)" for All Field search. For the second objective, which aimed to explore the mechanisms underlying heart rate regulation influenced by garlic, the search strings were "((garlic[MeSH Terms]) OR (allium[MeSH Terms])) AND (heart rate[MeSH Terms]) AND (gene[MeSH Terms])" for MeSH Terms, and "((“garlic”) OR (“allium”) OR (“allicin”)) AND (“heart rate”) AND (“gene”)" for All Field search.

Inclusion and exclusion criteria

The inclusion criteria comprised original research articles published in English from 2010 onward that investigated either changes in heart rate or the mechanisms influencing heart rate after administration of garlic, *A. sativum*, or allicin. Only studies that reported quantitative outcomes suitable for synthesis or meta-analysis were included. Studies were excluded if the full text was inaccessible, if duplicates were identified across databases, or if the publications consisted of reviews, commentaries, or conference abstracts without primary data.

Data extraction and analysis

Data extraction was performed independently by two reviewers, and discrepancies were resolved through discussion until consensus was reached. Extracted data included study characteristics, intervention details, and heart rate outcomes. For meta-analysis, the sample mean and standard deviation were used following the statistical approach described by (Chi et al., 2023).

RESULTS AND DISCUSSION

A total of 175 records were initially identified through the systematic search, of which 19 studies met the inclusion criteria for the qualitative synthesis and 13 were eligible for meta-analysis, as shown in Figure 1 (PRISMA Flowchart). The studies encompassed human clinical trials, experimental animal models, and *in vitro* mechanistic investigations, providing a broad and integrative perspective on the effect of garlic (*A. sativum*) and its principal bioactive compound, allicin, on heart rate (HR).

In human studies (summarized in Table 1.), garlic supplementation was generally associated with a modest reduction in HR. The pooled mean difference from the meta-analysis, approximately −5.57 ± 10.36 bpm (Table 4.), reflects a mild yet consistent bradycardic tendency across most trials. Notably, the study by Khastkhodaei et al. (2011) reported the greatest decrease (−14.95 bpm) after four weeks of daily organosulfur extract administration in patients with stable angina, whereas trials by Leitão et al. (2022) and Lopez et al. (2013) showed smaller or negligible effects in healthy or obese volunteers. Such differences are clinically meaningful and suggest that the chronotropic response to garlic is not uniform but instead depends heavily on the individual's cardiovascular condition and autonomic tone (Osailan et al., 2023). In subjects with heightened sympathetic activity, endothelial dysfunction, or ischemic heart disease, HR reduction may indicate a restoration of autonomic balance and vascular responsiveness. In contrast, individuals with normal cardiovascular regulation often exhibit minimal change, as homeostatic baroreflex mechanisms counteract further decreases in HR (Duong et al., 2020; Siepmann et al., 2022). This pattern aligns closely with previous studies on garlic's cardiovascular benefits, which consistently show that its blood pressure–lowering and endothelial effects are more pronounced in hypertensive than in normotensive populations (Ried et al., 2016; Wang et al., 2015). Collectively, these observations suggest that garlic's influence on HR likely represents part of a broader, adaptive cardiovascular modulation rather than a direct pharmacological suppression of cardiac rhythm.

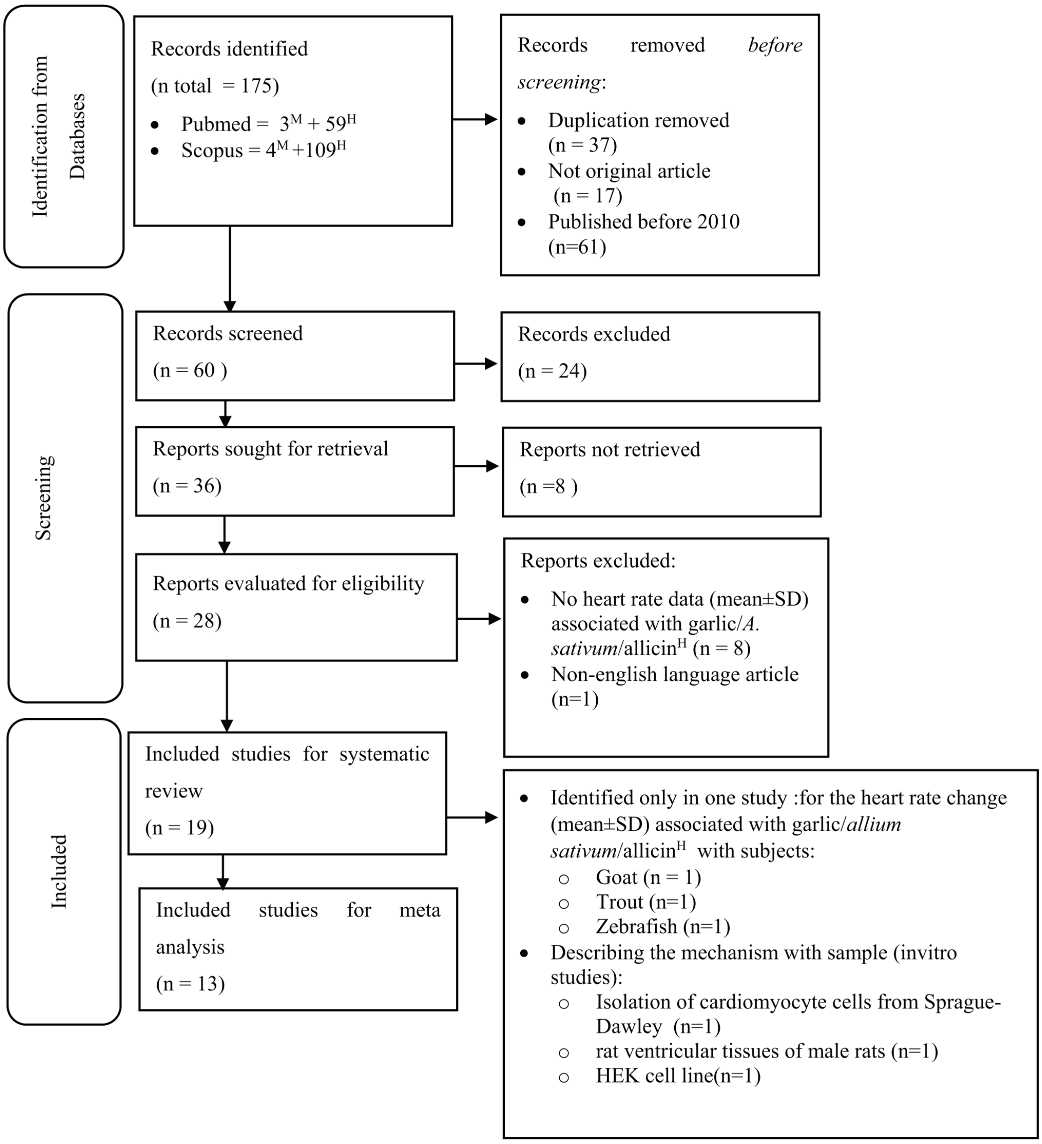

Figure 1. Prisma flowchart

^{M}= Records based on mechanism keywords (MeSH term and All Field), ^{H}= Records based on heart rate value keywords (MeSH term and All Field), HR = Heart Rate

Table 1. Characteristics of included studies in the systematic review for changes in heart rate value in human

Subject	Study (Author, year, country, subject, method)	Garlic (dose), duration of treatment, N subject	Concomitant therapy	Outcome Heart rate	Other outcomes
Human					
	Khastkhodaei et al., 2011 • Iran • Patients with stable chest angina • RCT	• Garlic organosulfur extract • (407.4 mg/ml- 60 ml/day) • For four weeks • Ntotal=40	60 ml/day extract consisted of hawthtorn (44.44 mg/ml), ginger (14.8 mg/ml), bilberry (20.4 mg/ml), red pepper (9.3 mg/ml), chammomile (14.8 mg/ml), willow bark (26.6 mg/ml)	Pre: 87.55 ± 3.23 Post: 72.60 ± 3.00 ∆: -14.95 ± 4.41	Lower LDL triglyceride and total cholesterol level
	Leitão et al., 2022 • Brazil • Patients with stable chest angina • RCT Leitão et al., 2022 • Brazil • Patients with stable chest angina • RCT	• Age Garlic • (2,4 g/day), • N/A, • Ntotal=28	(-)	Pre: 66.30 ± 11.87 Post: 63.33 ± 10.03 ∆: -2.97 ± 15.54	Age garlic extract improved microvascular function in male (age: 67±6) with cardiovascular disease high risk factors
	Lopez et al., 2013 • USA • obese human with metabo diet (consisted of raspberry ketone, caffeine, capsaicin, gingerols, shogaols, *Citrus aurantium* and related alkaloids, B vitamins, and chromium) • RCT	• Garlic • (N/A) • • For eight weeks • • Ntotal=27	Thiamin, riboflavin, niacin, pyridoxine, methylcobalamin, biotin, patothenic acid, Chromium, raspberry ketone, caffeine, capsaicin, garlic, ginger, and *Citrus aurantium*	Pre: 70.1 + 8.2 Post: 70.1 + 8.4 ∆: +0.00 ± 11.74	• Increased weight loss program (from 94±23 to 92± 23kg) • Reduced systolic (from 119± 10 to 118±10 mmHg) and diastolic blood pressure (77±8 to 76 ±9mmHg)
	McCrea et al., 2015 • USA • Healthy subject with obese • RCT	• Garlic powder • (1.81 gram) • • N/A • • N total = 20	Black pepper (0.91g), cinnamon (1.11g), cloves (0.61g), ginger (1.51g), oregano (2.26g), paprika (2.85g), rosemary (0.61g), turmeric (2.79g)	Pre: 64.43 ± 1.56 Post: 64.98 ± 1.84 ∆: +0.00 ± 2.41	Significantly lower triglycerides level by 31% (p<0,05) at rest condition,.
	Morris et al., 2013 • USA • Healthy cyclist in hypoxia • Cohort	• Garlic bulb powder (4650 mg/day) • • For 7 days • • N total=9	(-)	Pre: 183±10 Post: 182±11 ∆: -1.00 ± 14.87	No significant effect on oxygen consumption/saturation, peripheral blood pressures (both in exercise or resting condition), or exercise performance.

HR=heart rate; D HR=pre-post (result after garlic administration=minus (showed the HR reduction) or plus (demonstrated HR increase); D HR data was collected from the existing study or calculated based on formula proposed by Chi et al. (2023) and Arifin (2014); post and pre=after and before garlic administration; (-); No concomitant therapy with other treatment.

Animal studies presented in Table 2 showed a more robust HR reduction, with a pooled mean difference of approximately −50.06 ± 21.25 bpm (Table 5.). Studies in hypertensive, ischemic, or oxidative-stress-induced models demonstrated marked bradycardic responses after garlic or allicin administration, suggesting that the effect intensifies under pathological conditions characterized by sympathetic overactivation and oxidative stress (Grassi & Drager, 2024). In contrast, studies in normotensive or healthy animals showed smaller reductions or even transient HR increases at specific doses, underscoring that the effect is context- and concentration-dependent rather than universally bradycardic. Aqueous and aged garlic extracts, rich in stable organosulfur compounds, showed stronger HR-lowering effects than oil-based or ethanol extracts, which may contain different allicin derivatives. Excessively high doses sometimes produced paradoxical effects, possibly due to compensatory sympathetic activation or receptor desensitization. These inconsistencies instead reflect the pharmacodynamic complexity of garlic, a feature commonly observed in natural products, where multiple bioactive constituents may interact synergistically or antagonistically depending on dose and matrix composition (Sharma & Rani, 2021; Thomson et al., 2015).

Table 2. Characteristics of included studies in the systematic review for changes of heart rate value in rats

Subject	Study (Author, year, country, subject)	Garlic (dose), duration of treatment/evaluation period, N subject	Concomitant therapy	Outcome Heart rate	Other outcomes
Sprague-Dawley rats					
	Al-Qattan et al., 2017 • Kuwait • 2-kidney 1-clip rat model	• Raw garlic aqueous extract (30 mg / 100 g weight) • Five time i.v. administration of garlic • N=11	(-)	Pre: 188 ± 2 Post: 187 ± 1 Δ: -1.00 ± 2.24	Blocked angiotensin I converting enzyme dipeptidase activity and Angiotensin II generation
	Li et al., 2012 • China • cardiac hypertrophy rats	• Allicin 180 mg/kg/day • For 8 weeks • N=9	(-)	Pre: 321±15.6 Post: 306±17.6 D: -15.00 ± 23.53	Allicin inhibits the development of cardiac remodeling and cardiac hypertrophy, caused by increasing activity of Nrf2 antioxidant signaling pathways
	Manosroi et al., 2013 • Thailand • hypertensive Sprague-Dawley rats	• Extract garlic in water fraction (6.26 mg/kg) • After an administration the extract • N=6	(-)	D HR: -7.00±1.30	Reducing mean arterial blood pressure
	Manosroi et al., 2013 • Thailand • hypertensive Sprague-Dawley rats	• Extract garlic in butanol fraction (0.33 mg/kg) • After an administration the extract • N=6	(-)	D HR: -3.33±0.56	
	Manosroi et al., 2013 • Thailand • hypertensive Sprague-Dawley rats	• Extract garlic in ethyl acetate • (0.27 mg/kg) • After an administration the extract • N=6	(-)	D HR: +0.50±0.50	

Subject	Study (Author, year, country, subject)	Garlic (dose), duration of treatment/evaluation period, N subject	Concomitant therapy	Outcome Heart rate	Other outcomes
Sprague-Dawley rats					
Wistar rats					
	Asdaq et al., 2011 -India -rat with heart failure	• Extract garlic • (125 mg/kg BB) • • For 3 weeks • • N=8	(-)	Pre: 398.4 ± 3* Post: 353.2 ± 1 D: -44.20 ± 3.16	Lowering systolic blood pressure, cholesterol, triglycerides, glucose in HF rats.
		• Extract garlic (250 mg/kg BB) • For 3 weeks • • N=8	(-)	Pre: 398.4 ± 3 Post: 353.2 ± 1 D: -66.30 ± 3.16	
		• Extract garlic (500 mg/kg BB) • For 3 weeks • N=8	(-)	Pre: 398.4 ± 3 Post: 353.2 ± 1 D: -50.80 ± 3.61	
	Brankovic et al., 2011 • Serbia • Normotensive rat	• Garlic extract in ethanol • (6 mg/kg weight) • After an i.v. injection of the extract • N=6	(-)	Pre: 293 ± 10.76 Post: 196.31 ± 18.36 D: 96.69 ±21.28	Reducing arterial blood pressure
	Nwokocha et al., 2011 • Nigeria • Normotensive rat	• Aqueous garlic extract (20 mg/kg weight) • N=6	(-)	Pre: 378 ±5 Post: 207 ±5 D: 171 ±7.07	Decreasing blood pressure
	Nwokocha et al., 2011 • Nigeria • Hipertensive rat	• Aqueous garlic extract (20 mg/kg weight) • After garlic extract administration • N=6	(-)	Pre: 406 ±6 Post: 250 ±5 D: 156 ±7.81	Decreasing blood pressure
	Shackebaei et al., 2010 • Iran • Rat with Ischemia	• Garlic juice (0.01 mg/ml) was added to the perfusion solution 20 min before ischemia • After the hearts were perfused with the juice • (N=8)	(-)	Pre: 253 ± 10.27 Post: 217 ± 18 D: -36 ± 20.72	Improving on Rate pressure product and left ventricular developed pressure.
		• Garlic juice (0.01 mg/ml) was added to the perfusion solution min before and 10 min after ischemia • After the hearts were perfused with the juice • (N=7)	(-)	265 ± 13 227 ± 7.6 D: -38 ± 15.06	

Subject	Study (Author, year, country, subject)	Garlic (dose), duration of treatment/evaluation period, N subject	Concomitant therapy	Outcome Heart rate	Other outcomes
Sprague-Dawley rats					
	Supakul et al., 2014 • Thailand • Obese insulin-resistant rat	• Normal diet (250 mg/kg weight) • • For 28 days • (N=8)	(-)	Pre: 324 ± 24 Post: 311.05 ± 40 D: -12.95 ± 46.65	Decreasing plasma insulin, oxidative stress levels, and total cholesterol
		• Normal diet (500 mg/kg weight) • For 28 days • (N=8)	(-)	Pre 324 ± 24 Post: 333 ± 39 D: +9±45.79	
		• High fat diet (250 mg/kg weight) • For 28 days • (N=8)	(-)	Pre: 419 ± 3 Post: 307 ± 27 D: -112 ±27.17	
		• High fat diet (500 mg/kg weight) • For 28 days • (N=8)	(-)	Pre: 419 ± 3 Post: 315 ± 19 D: -104±19.24	

HR=heart rate; D HR=pre-post (result after garlic administration=minus (showed the HR reduction) or plus (demonstrated HR increase); D HR data was collected from the existing study or calculated based on formula proposed by Chi et al., (2023) and Arifin (2014); post and pre=after and before garlic administration; (-); No concomitant therapy with other treatment. i.v.= intravenous

Cross-species evidence summarized in Table 3 supports the consistency of this physiological trend. Experiments involving goats, trouts, and zebrafish all demonstrated significant HR reductions after garlic or allicin exposure. In zebrafish, for example, exposure to increasing concentrations of fresh garlic juice resulted in a dose-dependent decline in HR, ranging from 36 to 60 bpm reductions, which supports a conserved electrophysiological mechanism across vertebrates. Such findings reinforce the notion that garlic exerts a fundamental modulatory effect on cardiac pacemaker function rather than acting solely through secondary systemic changes.

Table 3. Characteristics of included studies in the systematic review for changes of heart rate value in goats, trouts, zebrafish

Subject	Study (Author, year, country, subject)	Garlic (*Allium sativum*)/Allicin (dose, N subject)	Concomitant therapy	Outcome Heart rate (HR)	Other outcomes
Goats,	Attia et al., 2021 • Egypt • One year old goat infected with with Escherichia coli	Allicin (2.7 mg /kg) twice a day at 12-h intervals for 42 days (N=4)	(-)	Pre: 104.0 ± 3.786 Post: 89.67 ± 2.728 Δ HR: 14.33 ± 4.67	Administration of allicin led to higher release of IL-6, IL-12, and TNF-α in both infected groups than in the untreated control
Trout	Papadopoulou et al., 2022 • Finland • Trout	• Allicin • (1000 mg/ml) for 6 weeks • (N=18)	(-)	Pre: 158.4 ± 4.70 Post: 143.6 ± 8.45 Δ HR: 14.80 ± 9.67	Alicin reduced the temperature coefficient of heart rate
Zebrafish	Majewski et al., 2017 • Poland • Zebrafish	Fresh garlic juice (0.01%) for 36 hours (N=7)	(-)	Pre: 131.60 ± 3.20 Post: 95.6 ± 9.7 Δ HR: 36.00 ± 10.21	Slow growth, swelling around the heart with heart defects, yolk deformities, absence of color, and body shape abnormalities have been observed at a level of 0.03% after 48 hours of exposure.
Zebrafish	Majewski et al., 2017 • Poland • Zebrafish	Fresh garlic juice (0.02%) for 36 hours (N=7)	(-)	Pre: 131.6 ± 3.2 Post: 84.9 ±7.3 Δ HR: 46.70± 7.97	Mortality was also higher with garlic exposure after being in contact for 12 hours at a level of 0.08%
Zebrafish	Majewski et al., 2017 • Poland • Zebrafish	Fresh garlic juice (0.03%) for 36 hours (N=7)	(-)	Pre: 131.6 ± 3.2 Post: 71.6 ± 4.7 Δ HR: 60 ± 5.69	

HR=heart rate; D HR=pre-post (result after garlic administration=minus (:showed the HR reduction) or plus (demonstrated HR increase); D HR data was collected from the existing study or calculated based on formula proposed by Chi et al., (2023) and Arifin (2014); post and pre=after and before garlic administration; (-); No concomitant therapy with other treatment; (-); No concomitant therapy with other treatment.

Mechanistic studies summarized in Table 6 offer crucial insight into why garlic and allicin lower HR. Chen et al. (2021) found that allicin significantly suppressed the late sodium current (INa,L) mediated by Nav1.5 channels in HEK293 cells expressing the KPQ-SCN5A mutation. This action stabilizes the cardiac action potential and reduces excitatory currents that drive arrhythmogenic and tachycardic responses. Similarly, Han et al. (2019) demonstrated that allicin inhibits Cav1.2 L-type calcium channel trafficking in rat ventricular tissues, reducing calcium influx and consequently decreasing sinoatrial node firing and contractility. Moreover, modulation of HCN4 expression further dampens sinoatrial node automaticity, providing a direct molecular rationale for HR reduction (Trieu et al., 2020). The same study reported that the ethyl acetate fraction of garlic produced the opposite effect, upregulating HCN4 expression and increasing beating rate, emphasizing that garlic's chronotropic effect is highly dependent on chemical composition and extraction solvent (Bar et al., 2022). This variability corresponds to the inconsistent results among studies in Tables 1–3, where certain extracts or doses caused minimal or paradoxical HR increases.

Table 4. Heart rate change after garlic administration in humans

Study	N Each study	Δ HR Each study	Ntotal	Δ HR total
Garlic treatment as single or in mixture ingredient				
Khastkhodaei et al., 2011	40	-14.95 ± 4.40	124	-5.57 ± 10.36
Leitão et al., 2022	28	-2.97 ±15.54		
Lopez et al., 2013	27	-0.00 ± 11.74		
McCrea et al., 2015	20	-0.00 ± 2.41		
Morris et al., 2013	9	-1.00 ± 14.86		
Garlic treatment as single ingredient				
Leitão et al., 2022	28	-2.97 ±15.54	37	-2.49 ± 15.39
Morris et al., 2013	9	-1.00 ± 14.86		

HR=heart rate; D HR=pre-post (result after garlic administration=minus (showed the HR reduction) or plus (demonstrated HR increase), classified into: D HR each study and D HR total [combining data (mean and standard deviation (using formula proposed by Axon et al., 2023 and Chi et al., 2023) from multi arm studies)]

Table 5. Heart rate change after garlic administration on rats

Study		N Each study	Δ HR Each study	Ntotal	Δ HR total
Sprague-Dawley rats					
Al-Qattan et al., 2017		11	-1.00 ± 2.24	29	-2.14 ± 1.56
Manosroi et al., 2013*	I	6	-7.00 ± 1.30		
	II	6	-3.30 ± 0.56		
	III	**6**	**-0.50 ± 0.50**		
Winstar rat				89	-61.25 ± 24.23
Asdaq et al., 2011*	I	8	-44.20 ± 3.16		
	II	8	-66.30 ± 3.16		
	II	8	-50.80 ± 3.61		
Brankovic et al., 2011		6	-96.69 ± 21.28		
Nwokocha et al., 2011*	I	6	-171 ± 7.07		
	II	6	-156 ± 7.81		
Shackebaei et al., 2010*	I	8	-36 ± 20.73		
	II	7	-38 ± 15.06		
Supakul et al., 2014*	I	8	-12 ± 46.65		
	II	8	+9 ± 45.79		
	III	8	-112 ± 27.17		
	IV	8	-104 ± 19.24		

HR=heart rate; D HR=pre-post (result after garlic administration=minus (showed the HR reduction) or plus (demonstrated HR increase), classified into: D HR each study and D HR total [combining data (mean and standard deviation) (using formula proposed by Axon et al., 2023 and Chi, 2023) from multi arm studies)]

Taken together, the evidence suggests that the HR-lowering activity of garlic and allicin is multifactorial. At the molecular level, the modulation of ion channels (Nav1.5, Cav1.2, HCN4) directly influences pacemaker automaticity and conduction velocity, producing negative chronotropy. On a systemic level, garlic enhances parasympathetic (vagal) tone, promotes vasodilation through improved nitric oxide bioavailability, and exerts antioxidant and anti-inflammatory actions that reduce sympathetic drive (Imaizumi et al., 2023). These pathways are interconnected: vasodilation reduces peripheral resistance and cardiac afterload, which in turn lowers reflex sympathetic activity and slows HR. Additionally, reduction of oxidative stress stabilizes the cardiac redox state, preserving ion channel function and reducing excitatory arrhythmogenic potential. The observed outcome is a physiologically mediated reduction in heart rate, which appears to be associated with restoration of autonomic balance rather than direct cardiac suppression (Hasan et al., 2022).

Table 6. Mechanistic pathways involved in the heart rate–lowering effects of garlic

(Study), Country, Garlic, Experimental Approach,	**Mechanism associated with Heart rate**
(Trieu et al., 2020) • Vietnam • Garlic *n*-hexane/dichloromethane/ethyl acetate extract, • Procedure: • ▸ Isolation of cardiomyocyte cells from Sprague-Dawley rat (1- to 2-day-old) • ▸ Inducing beating rate • ▸ HCN4 expression	Beating rate and HCN4 expression ▸ Garlic extract in n-hexane and dichloromethane (20 µg/mL) demonstrated lower beating rate and HCN4 expression than negative control groups ▸ Garlic ethyl acetate extract (20 µg/mL) showed higher beating rate and HCN4 expression than negative control groups
(Chen et al., 2021) • China, • Allicin, • Procedure: • ▸ Cell culture and transfection, Confocal Imaging, Western Blotting (HEK 293 cell line, ΔKPQ-SCN5A mutations) • ▸ Electrophysiological and current Recordings	Allicin (30 mM) significantly reduced the late sodium current (Ina,L) of the Nav1.5 channel current which encoded by 1KPQ-SCN5A,
(Han et al., 2019) • China, • Allicin, • Procedure: • ▸ Cell culture, Cell viability determination (ventricular tissues of male rats aged 5–8 weeks) • ▸ Cav1.2 protein expression	Allicin caused trafficking dysfunction, which resulted in the inhibition of cardiac Cav1.2 channels

When contextualized within broader literature, these findings align with a growing body of evidence on the cardioprotective and autonomic regulatory effects of garlic. Reviews by El-Saadony et al. (2024), Gao et al. (2024), and Li et al. (2023) have outlined garlic's ability to modulate oxidative stress, lipid peroxidation, and vascular inflammation, processes closely linked to autonomic function and HR control. Taken together, these studies reinforce that the HR-lowering property of garlic is mechanistically coherent with its other cardiovascular actions. HR reductions have been reported following administration of both complex garlic preparations/extracts and isolated allicin; however, the relative contribution of allicin is likely formulation-dependent due to its chemical instability and rapid conversion to downstream organosulfur metabolites. Consequently, preparations with different organosulfur profiles and allicin-generating capacity may produce HR effects through overlapping but not identical pathways. At the same time, they highlight critical research needs: improved extract standardization, standardized reporting of key chemical markers (including allicin content/yield and other relevant organosulfur constituents), identification of key bioactive sulfur compounds responsible for autonomic modulation, and pharmacokinetic data defining effective human dosing.

Despite the consistency of these physiological trends, the strength of evidence remains limited by methodological weaknesses across included studies. Many human trials were small, single-center, and lacked details on randomization, blinding, or the chemical standardization of extracts. In several studies, intervention characterization was insufficient (e.g., absence of standardized marker reporting such as allicin content/yield or comparable organosulfur profiling), which limits inference regarding whether HR changes were driven by allicin specifically or by other constituents/metabolites present in the extract matrix. Similarly, most animal experiments did not report allocation methods or blinding of outcome assessment. These methodological shortcomings introduce potential bias that could either exaggerate or underestimate true effects. Therefore, the present findings should be interpreted with appropriate caution. Future systematic reviews should incorporate formal risk-of-bias assessment frameworks and ideally apply GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria to evaluate certainty of evidence.

CONCLUSION

This systematic review and meta-analysis provide comprehensive evidence that garlic (*A. sativum* L.) and its active compound allicin exert a heart rate–lowering effect across human, animal, and cellular models. The HR reduction appears to be mediated through multiple pathways, including modulation of sodium and calcium channel currents, downregulation of HCN4 expression, enhancement of parasympathetic tone, and attenuation of oxidative stress. Nonetheless, the extent of HR modulation is dose-dependent and influenced by extract type and physiological condition, suggesting that garlic acts as a functional modulator rather than a fixed chronotropic agent. Notably, this study offers a novel contribution by quantitatively synthesize heart rate–specific outcomes while integrating mechanistic evidence to distinguish formulation- and pathway-dependent effects of garlic and allicin, thereby addressing inconsistencies in prior cardiovascular-focused reviews. These findings strengthen the scientific basis for garlic's cardioprotective properties and highlight its potential as an evidence-based herbal adjunct in cardiovascular therapeutics. Further well-controlled clinical studies are warranted to optimize formulation, dosage, and treatment duration for maximal efficacy and safety.

AUTHOR CONTRIBUTION STATEMENT

RR: Concept and design, drafting the manuscript, supervision, final approval; RN: Concept and design, data analysis, drafting the manuscript, critical revision of the manuscript, final approval

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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