Flavanones from *Citrus sinensis* L. (Fruit): A Natural Innovation for Sports Nutrition, Health, and Wellness Formulations

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ABSTRACT

Citrus sinensis flavanones (hesperidin and narirutin) enhance athletic performance and cardio-metabolic health, as evidenced by clinical trials. Key benefits include improved oxidative stress, inflammation, and endothelial function. This review is a narrative compilation of randomized trials from reliable sources (PubMed, ScienceDirect, Publons, and Google Scholar) that investigate the impact of C. sinensis on athletic performance, oxidative stress management, inflammation, endothelial function, dyslipidemia, and hypertension. Hesperidin, either alone or in combination with narirutin, was found to enhance exercise output, increase anaerobic power, and positively impact key biomarkers of muscle fatigue, oxidative stress, and inflammation. Mechanistic insights include enhanced endogenous antioxidant capacity (SOD ↑ and DPPH ↑), downregulation of pro-inflammatory cytokines (TNF-α ↓, IL-6 ↓, hs-CRP ↓), and elevated endothelial function (FMD ↑, sICAM-1 ↓, and sVCAM-1 ↓). Notably, clinical interventions also resulted in significant improvements in blood pressure regulation and lipid profiles, with reductions in systolic and diastolic blood pressure, LDL-C, and triglycerides. These outcomes position *C. sinensis* as a promising natural agent to support athletic performance and cardiometabolic health, particularly in individuals engaged in prolonged/high-intensity exercise or those with metabolic disorders.

Keywords: *Citrus sinensis* flavanones, Hesperidin and narirutin, Sports nutrition, Oxidative stress management, Endothelial function improvement

Abbreviations

AUC-GSSG - Area under the curve-glutathione disulfide
MCP1 - Monocyte chemoattractant protein-1
DPPH - 2,2-diphenyl-1-picrylhydrazyl
FRAP - Ferric reducing antioxidant power
ORAC - Oxygen radical absorbance capacity
SOD - Superoxide dismutase
MDA - Malondialdehyde
TAC - Total antioxidant capacity
SBP - Systolic blood pressure
DBP - Diastolic blood pressure
HDL-C - High-density lipoprotein cholesterol
LDL-C - Low-density lipoprotein cholesterol
sVCAM-1 - Soluble vascular cell adhesion molecule 1
sICAM-1 - Soluble intercellular adhesion molecule 1
FMD - Flow-mediated dilation
hsCRP - High-sensitivity C-reactive protein
TNF-α - Tumor necrosis factor-alpha
RCTs - Randomized controlled trails
SAA - Serum amyloid A
BMI - Body mass index
AI - Artificial intelligence

Introduction

Intense exercise elevates reactive oxygen species, leading to oxidative stress and muscle damage.[1–3] To mitigate these effects, *Citrus sinensis* flavanones have gained prominence in sports nutrition due to their multifaceted bioactivities.[4,5] Hesperidin and narirutin hold the potential to suppress the generation of free radicals, downregulate pro-inflammatory cytokines, support vasodilatory properties, and mitochondrial biogenesis, which are highly pertinent to athletic performance and recovery.[3,6–9]

The bioavailability and stability of flavanones enable them to exert systemic effects even at dietary doses.[10,11] Moreover, these compounds aid in recovery by modulating inflammatory pathways, reducing markers such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which are often elevated after intense training sessions.[3,12] Given the growing emphasis on natural performance-enhancing strategies, the integration of *C. sinensis* flavanones into sports nutrition represents a novel and evidence-based approach. However, this narrative review critically examines the available clinical evidence, focusing on C. sinensis flavanones and providing mechanistic insights, while also aiming to guide future research and formulation strategies in the sports nutrition, as well as health and wellness sectors.

Methodology

This narrative review synthesizes evidence from clinical trials investigating *Citrus sinensis* flavanones (hesperidin and narirutin) in the context of sports nutrition and cardio-metabolic health. Literature was sourced from PubMed, ScienceDirect, Google Scholar, and Publons (2010–2023) using keywords: *"hesperidin," "narirutin," "athletic performance," "oxidative stress," "endothelial function," "hypertension,"* and *"dyslipidemia."*

Inclusion Criteria

- **Design:** Randomized controlled trails (RCTs), crossover, or controlled cohort studies.
- **Population:** Humans (athletes, healthy/overweight adults, or metabolic patients).
- **Intervention:** *C. sinensis* extracts, orange juice, or isolated hesperidin/narirutin.
- **Outcomes:** Biomarkers, performance metrics, or clinical endpoints.

Exclusion Criteria

- Non-human/in vitro studies.
- Non-English or inaccessible full texts.
- Studies lacking placebo controls or dosing details

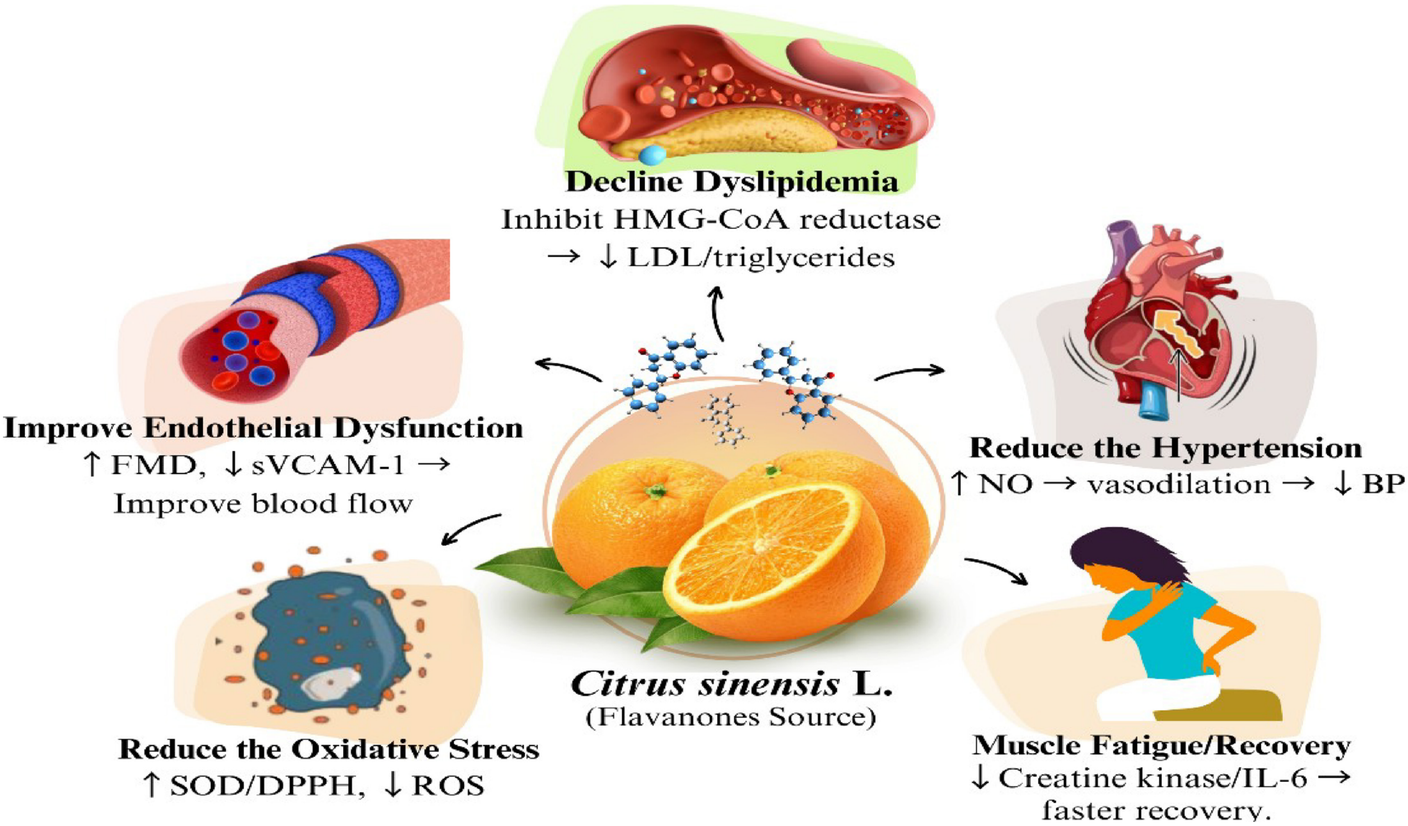

Fig 1 | Mechanisms of hesperidin and narirutin in sports nutrition, oxidative stress, inflammation, endothelial function, dyslipidemia, and hypertension

Health Promoting Aspects

C. sinensis flavanones are widely discussed below for health-promoting properties across a range of clinical trials as presented in Table 1. Moreover, key mechanisms involved are outlined in Figure 1.

Athlete's Performance

C. sinensis flavanones, mainly hesperidin and narirutin, have the potential to demonstrate significant impacts in elevating sports nutrition and performance.

A recent clinical trial reported that the intake of hesperidin alone or in combination with narirutin improved physical endurance/stamina, muscle performance, and reduced oxidative stress.[13] Similarly, in amateur cyclists, hesperidin intake showed favorable changes in body composition by increasing muscle mass and reducing fat mass.[3] Intake of *C. sinensis* fruit extract wherein 90% was hesperidin (360–450 mg/day for 8 weeks) also improved performance in 61 trained athletes, increasing their anaerobic power and speed in the Wingate test.[14] Overdevest et al.[15] reported that the intake of *C. sinensis* fruit extract containing 90% hesperidin (450 mg/day of hesperidin over a period of 4 weeks) increased absolute power output by 5% and reduced oxygen consumption in subjects while cycling, who were 19 in total. In another study by Martínez-Noguera et al.,[16] the dose of 500 mg/day of hesperidin increased performance in anaerobic exercises, such as cycling, in 15 participants. Moreover, pre-exercise supplementation of 217 mg of hesperidin and 230 mg of narirutin per soccer player minimized oxidative stress and muscle damage during the Yo-Yo test while maintaining their performance.[17] In another clinical trial, intake of 300 mL hesperidin and narirutin-rich orange juice for 12 days added valuable insights about exercise-induced physiological responses, particularly in combat sport athletes like those practicing *Tarung Derajat*. Intake reduced creatinine kinase levels and significantly impacted leukocyte count reduction post-training, suggesting an immunomodulatory or anti-inflammatory effect in response to exercise stress. These results strongly support the potential role of *C. sinensis* flavanones in enhancing athletic endurance, recovery, and physical performance.[18]

Oxidative Stress Management

Elevating the endogenous defense system through the intake of antioxidant supplements may represent an effective non-invasive tool for mitigating or reducing oxidative stress during training. As noted earlier, exercise-induced oxidative stress damages cellular components.[19] *C. sinensis* flavanones counteract this via enhanced antioxidant capacity (e.g., SOD ↑) and reduced lipid peroxidation.

In a recent study, Martínez-Noguera et al.[13] investigated the impact of supplementing with hesperidin at a dose of 500 mg/day for 8 weeks in 20 cyclists. Results showed a considerable decrease in oxidative stress and

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Table 1 | Clinical trial evidence of *C. sinensis* flavanones across health domains

Flavanone/Dose/Duration	Participants	Findings	References
		Athletic Performance	
Hesperidin/500 mg/day for 8 weeks	20 cyclists, while the Rectangular Test and Maximal Test	↑ SOD, $p < 0.05$ ↓ MCP1, $p < 0.01$	Martínez-Noguera et al.[13]
Hesperidin/500 mg/day for 8 weeks	20 amateur competitive cyclists	↑ Muscle mass, $p = 0.03$ ↓ Fat mass, $p = 0.02$	Noguera et al.[3]
Hesperidin/360 and 450 mg/day for 8 weeks	61 trained athletes	↑ Anaerobic performance, $p = 0.004$ ↑ Speed, $p < 0.01$	van Iersel et al.[14]
Hesperidin/450 mg/day for 4 weeks	19 trained athletes, while 10 10-minute time-trials on a cycle ergometer	↑ Power output by 5%, $p = 0.02$ ↓ Oxygen consumption/power ratio, $p < 0.01$	Overdevest et al.[15]
Hesperidin/500 mg/day	15 cyclists	↑ Average power by 2.27%, $p = 0.023$), ↑ Max speed by 3.23%, $p = 0.043$, ↑ Total energy by 2.64%, $p = 0.028$	Martínez-Noguera et al.[16]
Hesperidin (217 mg) and narirutin (230 mg)/2.5 h before test	11 soccer players, while the Yo-Yo intermittent recovery test	↓ Muscle damage, $p < 0.05$ ↓ Oxidative stress, $p < 0.05$	Boussetta et al.[17]
300 mL orange juice/day for 12 days m	10 athletes practicing ***Tarung Derajat***	↓ Creatinine kinase levels, $p = 0.296^{ns}$ ↓ Count of leukocytes, $p = 0.005$	Siregar et al.[18]
		Oxidative Stress	
750 mL orange juice Hesperidin 103 mg/L and narirutin 15 mg/L/day for 8 weeks	21 normal overweight subjects	↓ MDA 2.4 → 1.5 μM, $p = 0.001$ ↑ DPPH 8.8% → 26.5%, $p < 0.001$	Dourado and Cesar[6]
600 mL of orange juice Hesperidin 213 mg and narirutin 29 mg/day for 4 weeks	25 males with cardiovascular risk	↑ FRAP +84.6 μmol/L, $p < 0.05$ ↑ ORAC +1.25 mmol/L, $p < 0.05$	Constans et al.[20]
500 mg/day hesperidin for 6 weeks	64 patients with type 2 diabetes	↑ TAC 0.7 → 0.8 mM, $p = 0.03$	Homayouni et al.[7]
		Hypertension	
Hesperidin enriches orange juice (500 mg/day) and narirutin (77.5 mg/day) for 12 weeks	159 hypertensive subjects of pre- and stage-1	↓ SBP (−7 mmHg), $p < 0.001$ ↓ Pulse pressure, $p = 0.01$	Valls et al.[21]
Hesperidin (582 mg/day) and narirutin (125 mg/day) for 12 weeks	100 nonsmoking obese individuals	↓ SBP (−4 mmHg), $p = 0.02$, ↓ DBP (−5 mmHg), $p = 0.01$	Rangel-Huerta et al.[22]
Hesperidin (292 mg) and narirutin (47 mg)/day for 4 weeks	24 healthy and overweight	↓ DBP, $p = 0.02$	Morand et al.[8]
Hesperidin (600 mg/day) for 12 weeks	159 hypertensive individuals	↓ SBP (−3.2 mmHg)_ $p = 0.02$	Pla-Pagà et al.[23]
Hesperidin (500 mg/day) for 12 weeks	49 patients with metabolic syndrome	↓ SBP (−2.68 mmHg), $p = 0.03$ ↑ HDL-C (+2 mg/dL), $p = 0.04$	Yari et al.[24]
Hesperidin 450 mg/day for 6 weeks	68 healthy overweight individuals	↓ SBP (−5 mmHg), $p = 0.051$ ↓ DBP (−2 mmHg), $p = 0.069$	Salden et al.[9]
Hesperidin 500 mg/day for 6 weeks	64 patients with type 2 diabetes	↓ DBP (−4 mmHg), $p = 0.005$ ↓ SBP (−3 mmHg), $p = 0.006$	Homayouni et al.[12]
Hesperidin 320 mg/day for 4 weeks	16 patients	↓ SBP (−3 mmHg), $p < 0.05$ ↓ DBP (−5 mmHg), $p < 0.05$	Schär et al.[25]
		Cardiovascular Health	
Hesperidin 450 mg/day for 6 weeks	68 individuals	↓ sVCAM-1, $p = 0.001$ ↓ sICAM-1, $p = 0.003$ ↓ sP-selectin, $p < 0.05$	Salden et al.[9]
Hesperidin (292 mg) and narirutin (47 mg)/day for 4 weeks	24 healthy and overweight	↑ Endothelial reactivity by +2.1%, $p = 0.04$ ↓ Postprandial sVCAM-1, $p < 0.05$	Morand et al.[8]
Hesperidin 500 mg/day for 3 weeks	24 individuals with metabolic syndrome	↑ FMD by 10.26%, $p = 0.001$	Rizza et al.[26]
Hesperidin 600 mg/day for 4 weeks	75 patients with myocardial infarction	↑ HDL-C by +24%, $p = 0.01$ ↓ LDL-C by −16%, $p = 0.02$	Haidari et al.[27]
Hesperidin (500 mg/day) for 12 weeks	49 patients with metabolic syndrome	↑ HDL-C, i.e., good cholesterol, from 35 to 37 (mg/dL) ↓ LDL-C, i.e., bad cholesterol, from 118 to 105 (mg/dL), $p < 0.05$ ↓ Triglycerides from 185 to 136 mg/dL, $p < 0.05$ ↓ Total cholesterol from 181 to 163 mg/dL, $p < 0.05$	Yari et al.[24]
750 mL orange juice, Hesperidin 103 mg/L and narirutin 15 mg/L/day for 8 weeks	21 normal overweight subjects	↓ Triglycerides from 89 to 84 (mg/dL), $p = 0.12$ ↓Total cholesterol from 173 to 159 (mg/dL), $p = 0.021$ ↓ LDL-C, i.e., bad cholesterol, from 104 to 93 (mg/mL), $p = 0.015$	Dourado and Cesar[6]

Continued

Table 1 | Continued

Flavanone/Dose/Duration	Participants	Findings	References
300 mL/day for 60 days, 73 mg hesperidin +15 mg narirutin	10 individuals	↓ LDL-C, i.e., bad cholesterol (−16%), $p < 0.05$ ↓ Triglycerides (−30%), $p < 0.05$	Fidélix et al.[28]
		Anti-inflammatory Effects	
Hesperidin 500 mg/day for 3 weeks	24 individuals with metabolic syndrome	↓ hs-CRP (3.9 ⇢ 2.6 mg/L), $p = 0.001$ ↓ Serum amyloid A (SAA) (7.3 ⇢ 5.6 mg/L), $p < 0.05$	Rizza et al.[26]
Hesperidin 600 mg/day for 4 weeks	75 patients with myocardial infarction	↑ adiponectin (mg/L) around 23%, $p < 0.05$ ↓ E-selectin (ng/mL), IL-6 (pg/mL), hs-CRP (mg/L), and Leptin (ng/mL) around −18%, −68%, −70%, and −50%, respectively, $p < 0.05$	Haidari et al.[27]
Hesperidin (500 mg/day) for 12 weeks	49 patients with metabolic syndrome	↓ hs-CRP by 45%, $p = 0.01$	Yari et al.[24]
500 mg/day hesperidin for 6 weeks	64 patients with type 2 diabetes	↓ TNF-α (18.7 ⇢ 17 ng/mL), $p = 0.04$), ↓ IL-6 (8.3 ⇢ 7.4 ng/L), $p = 0.03$	Homayouni et al.[12]
Hesperidin 103 mg/L and narirutin 15 mg/L/day for 8 weeks	21 normal overweight subjects	↑ IL-12 (pg/mL), $p < 0.05$ ↓ TNF-α from 21.5 to 19.1 (pg/mL), $p < 0.05$ ↓ hs-CRP from 0.25 to 0.12 (mg/dL), $p < 0.05$	Dourado and Cesar[6]

an impressive increase in the superoxide dismutase (SOD) levels. Moreover, a decline was also observed in oxidative stress (AUC-GSSG) and inflammatory monocyte chemoattractant protein-1 (MCP1) markers during cycling performance tests. The intake of orange juice (750 mL), which delivers approximately 103 mg/L hesperidin and 15 mg/L narirutin, resulted in a notable decline in malondialdehyde (MDA) levels, from 2.4 to 1.5 µM, in overweight individuals, indicating a reduction in lipid peroxidation. Likewise, antioxidant capacity, as measured by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, improved from 8.8 to 26.5%.[6] Added that, intake of orange juice (600 mL) in subjects with cardiovascular risk factors outlined increased plasma antioxidant markers, including Ferric Reducing Antioxidant Power (FRAP) (+84.6 µmol/L), Oxygen Radical Absorbance Capacity (ORAC) (+1.25 mmol/L), and β-cryptoxanthin (+0.23 µmol/L), depicting an enhancement of systemic antioxidant defense.[20] Also, hesperidin supplementation (500 mg/day) for 6 weeks in patients with type 2 diabetes improved total antioxidant capacity (TAC) from 0.7 to 0.8 mM.[7] Moreover, pre-exercise supplementation of 217 mg of hesperidin and 230 mg of narirutin per soccer player minimized oxidative stress during the Yo-Yo test while maintaining their performance.[17]

The consistent improvements in oxidative stress biomarkers position *C. sinensis* flavanones as a matchless ingredient for athletes, health, and wellness formulations.

Anti-Inflammatory Effects

Prolonged or high-intensity exercise results in the release of pro-inflammatory cytokines, mainly IL-6, which stimulates the release of hepatic high-sensitivity C-reactive protein (hs-CRP) and may contribute to muscle damage and delayed recovery.[29] *C. sinensis* flavanones consistently exhibit anti-inflammatory activities across various human clinical trials. At a dose of 500 mg/day, multiple studies reported reductions in hs-CRP, TNF-α, and MCP1, key biomarkers of systemic inflammation and muscle damage. For instance, Martínez-Noguera et al.[13] recorded a notable decline in MCP1 during cycling performance tests. Rizza et al.[26] observed reductions in hs-CRP (3.9–2.6 mg/L), serum amyloid A protein (7.3–5.6 mg/L), and soluble E-selectin (31–27 ng/mL). Similar effects were observed in a 12-week study by Yari et al.,[24] where hs-CRP levels decreased from 3691 to 2026 ng/dL and TNF-α levels decreased from 23 to 19 pg/mL. Homayouni et al.[12] reported comparable outcomes in patients with type 2 diabetes, with reductions in TNF-α (18.7–17 ng/mL), hs-CRP (1.9–1.1 mg/L), and IL-6 (8.3–7.4 ng/L) after 6 weeks. This dose-dependent consistency reinforces hesperidin's potential as a reliable anti-inflammatory agent. Haidari et al.[27] found increases in adiponectin (~23%) and marked reductions in E-selectin (−18%), IL-6 (−68%), hs-CRP (−70%), and leptin (−50%), indicating cardiovascular and metabolic regulatory benefits. Meanwhile, Dourado and Cesar[6] explored the impact of orange juice delivering 103 mg/L hesperidin and 15 mg/L narirutin for 8 weeks. Although the dose was lower, it still improved IL-12 production, i.e., a cytokine crucial for innate immunity. It decreased TNF-α (21.5–19.1 pg/mL) and hs-CRP (0.25–0.12 mg/dL), underscoring the functional value of *C. sinensis* flavanones in sports nutrition, health, and wellness.

Endothelial Function

Restricted blood supply to the muscles during strenuous exercise is thought to hinder muscle oxygenation.[30] For instance, it has been observed that restricted blood flow negatively affects the performance of speed skaters, as flow-mediated dilation (FMD) drops. A 1% increase in FMD is associated with a 9% decrease in heart risk. Dietary strategies, especially those rich in polyphenols, may be a helpful method to preserve endothelial health.[31–34] *C. sinensis* flavanones intake also offers cardio-protective effects through improved endothelial function and reduced vascular inflammation. Clinical trials also highlight hesperidin's anti-inflammatory and vascular benefits, particularly enhancing endothelial function and lowering markers of cardiovascular risk. In a 6-week trial involving 68 subjects, 450 mg/day hesperidin decreased the levels of major adhesion molecules, including soluble vascular cell adhesion molecule-1 (sVCAM-1), soluble intercellular adhesion molecule-1 (sICAM-1), and sP-selectin, which contribute to vascular inflammation.[9] Morand et al.[8] also observed improved postprandial endothelium-dependent microvascular reactivity in 24 healthy overweight individuals after daily consumption of orange juice with 292 mg of hesperidin and 47 mg of narirutin for 4 weeks. Rizza et al.[26] observed a significant improvement in FMD, a measure of endothelial function, in subjects with metabolic syndrome after taking 500 mg/day of hesperidin for 3 weeks.

Dyslipidemia

Daily consumption of 750 mL orange juice (delivering 103 mg/L hesperidin and 15 mg/L narirutin) for 2 months caused a notable decline in triglycerides (from 89 to 84 mg/dL), total cholesterol (173 to 159 mg/dL), and low-density lipoprotein cholesterol (LDL-C) (104 to 93 mg/dL), representing an overall improvement in lipid profiles among overweight subjects.[6] Likewise, Fidélix et al.[28] recorded similar results with an intake of 300 mL/day orange juice (delivering 73 mg hesperidin and 15 mg narirutin) for 2 months, causing a 16% reduction in LDL-C and a 30% drop in triglycerides from baseline. Collectively, data from the clinical trial position *C. sinensis* flavanones as a multi-target agent that positively influences lipid profile by integrating metabolic regulation with antioxidant and anti-inflammatory properties.

Hypertension

C. sinensis flavanones, including hesperidin and narirutin, have been clinically validated for their blood pressure-lowering properties. In a clinical trial involving 159 hypertensive participants, a dose of 600 mg per day of hesperidin, alongside 77.5 mg per day of narirutin, was able to reduce both systolic and diastolic blood pressure (DBP) by 7 mmHg, thereby achieving a reduction in pulse pressure.[21] Likewise, separate research with 100 obese non-smoking participants with an administered dose of 582 mg of hesperidin along with 125 mg of narirutin for 12 weeks showed not only a decrease of 4 mmHg in systolic blood pressure (SBP) and 5 mmHg in DBP but also a decrease in Body mass index (BMI), waist circumference, and serum leptin levels.[22] Furthermore, Morand et al.[8] reported that a 292 mg dose of hesperidin and 47 mg of narirutin enriched orange juice consumed over a period of 4 weeks led to a reduction in the DBP in a group of 24 clinically examined healthy overweight men. Besides, Pla-Pagà et al.[23] reported a reduction in blood pressure levels and inflammatory markers in 159 subjects with hypertension after 12 weeks of treatment with a daily dose of 600 mg of hesperidin. Yari et al.[24] investigated the effects of a 12-week daily dose of 500 mg of hesperidin in a randomized interventional study on 49 subjects with metabolic syndrome, where the average decreases in systolic and diastolic pressure were 2.68 and 2 mmHg, respectively. Salden et al.[9] highlighted the response of 68 overweight individuals to the consumption of 450 mg/day of hesperidin for 6 weeks, demonstrating a reduction of 5 mmHg in systolic and 2 mmHg in diastolic pressure. Another study involving 64 subjects with type 2 diabetes observed a reduction of 4 mmHg in systolic and 1.8 mmHg in diastolic blood pressure after 6 weeks of 500 mg/day hesperidin supplementation.[12] Furthermore, Schär et al.[25] reported a reduction of 3 mmHg in systolic and 5 mmHg in diastolic pressure after taking red orange juice containing 320 mg of hesperidin for 4 weeks in subjects at moderate risk for cardiovascular diseases. A short-term trial by Rizza et al.[26] reported that 24 subjects with metabolic syndrome showed lower SBP and improved endothelial function after 3 weeks of 500 mg/day of hesperidin, further validating *C. sinensis* flavanones as a natural and effective support for blood pressure regulation and cardiovascular wellness.

Translational Applications

Clinically effective doses include 450–500 mg/day of hesperidin (4–8 weeks) for improving anaerobic performance, and 500–600 mg/day for managing hypertension. Acute recovery benefits are observed with 217 mg hesperidin +230 mg narirutin pre-exercise. Commercial applications span endurance formulations (pre-workout blends), recovery products, and functional foods. Standardization is critical, with a target of ≥90% hesperidin purity, a nano-emulsion formulation for enhanced bioavailability, and synergy with vitamin C for improved stability.

Conclusion

We found that *C. sinensis* flavanones, primarily hesperidin and narirutin, present compelling evidence of efficacy across a range of health domains relevant to sports nutrition and general wellness. These effects are particularly valuable not only for athletes seeking performance gains and faster recovery but also for the general population aiming to improve overall well-being. Given their natural origin, favorable safety profiles, and multifactorial bioactivity, *C. sinensis* flavanones are promising candidates for inclusion in functional foods, dietary supplements, and wellness formulations. However, to fully realize this potential, targeted research should address several key areas. First, advanced metabolomics and lipidomics approaches could elucidate personalized responses to supplementation. Second, machine learning/AI approaches may help develop bespoke flavanone combinations optimized for specific disease states or athletic needs. Third, the potential for tailored formulations targeting particular populations requires clinical validation. Fourth, long-term trials (>6 months) are necessary to evaluate the sustained effects on chronic conditions. Fifth, gut microbiota interactions warrant investigation to enhance the bioavailability of nutrients. Sixth, standardized delivery systems (e.g., nanoemulsions) must be tested to improve absorption. Finally, comparative studies against other polyphenols could clarify unique advantages. Addressing these gaps will advance precision applications in sports and metabolic medicine.

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