INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

LUTEOLIN IN CARDIOVASCULAR PHARMACOLOGY: IMPLICATIONS FOR PRINZMETAL ANGINA: A NARRATIVE REVIEW

Narrative Review

Sidra Sabir[1], Ishrat Younus[1]*, Tahmina Maqbool[2], Farzana Sadaf[1]
[1]Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan.
[2]Department of Pharmaceutics, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan.
Corresponding Author: Ishrat Younus, Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan, Mohammed Said Road, Karachi, Pakistan, Ishrat.imran@hamdard.edu.pk
Acknowledgement: The authors express their sincere gratitude to the Faculty of Pharmacy, Hamdard University, for their academic guidance and support throughout the development of this review. Special thanks are extended to all researchers whose contributions to the field of cardiovascular pharmacology provided the foundation for this study.

Conflict of Interest: None Grant Support & Financial Support: None

ABSTRACT

Background: Luteolin, a naturally occurring flavonoid abundantly found in various fruits, vegetables, and medicinal plants, has drawn increasing scientific attention due to its potent antioxidant, anti-inflammatory, and vasoprotective properties. Its pharmacological profile suggests therapeutic potential in cardiovascular diseases, particularly conditions characterized by endothelial dysfunction and vasospasm. Among these, Prinzmetal angina—a variant form of angina marked by transient coronary artery spasms—represents a clinical context in which luteolin's endothelial and vascular effects may have significant therapeutic relevance.

Objective: This narrative review aims to evaluate the pharmacological potential of luteolin in the management of Prinzmetal angina, emphasizing its mechanisms of action related to endothelial modulation, nitric oxide bioavailability, and vasodilatory response.

Main Discussion Points: The review synthesizes evidence showing that luteolin enhances endothelial nitric oxide production, mitigates oxidative stress, and inhibits inflammatory mediators such as TNF-α and IL-6, which collectively contribute to improved vascular tone and reduced vasospastic activity. It also discusses how luteolin's ability to regulate calcium channel activity and attenuate vascular smooth muscle contraction may counteract ischemic episodes characteristic of Prinzmetal angina.

Conclusion: Emerging evidence indicates that luteolin may reduce the frequency and severity of coronary vasospasms by restoring endothelial balance and suppressing inflammatory and oxidative mechanisms. While preclinical findings are encouraging, large-scale clinical trials are essential to establish its safety, efficacy, and therapeutic integration into angina management protocols.

Keywords: Luteolin, Prinzmetal Angina, Vasospastic Angina, Endothelial Dysfunction, Nitric Oxide, Cardiovascular Pharmacology.

INTRODUCTION

Luteolin is a naturally occurring flavonoid abundantly present in several fruits, vegetables, and herbs such as celery, broccoli, green bell peppers, navel oranges, dandelions, peppermint, and rosemary (1). Over the past few decades, flavonoids have gained prominence for their multifaceted roles in maintaining human health, with luteolin emerging as one of the most pharmacologically versatile among them. Extensive research has demonstrated its potent antioxidant, anti-inflammatory, antimicrobial, and anticancer effects, contributing significantly to its therapeutic reputation (2,3). Its biochemical mechanisms enable modulation of oxidative stress and inflammation, which are pivotal in the pathogenesis of numerous chronic diseases including cancer and cardiovascular disorders (4). Luteolin exerts its biological influence by targeting multiple molecular signaling pathways that regulate cellular proliferation, metastasis, and apoptosis within neoplastic tissues (5). Furthermore, it exhibits substantial cardioprotective activity by attenuating oxidative stress, restoring endothelial function, and modulating inflammatory mediators within the cardiovascular system (6). This dual capacity—anticancer and cardioprotective—makes luteolin a compound of considerable clinical interest. Recent epidemiological findings have linked higher dietary luteolin intake with a significant reduction in all-cause mortality, particularly cardiac-related deaths in patients with type 2 diabetes mellitus (T2DM), further emphasizing its potential role in chronic disease prevention (7,8). Despite this growing body of evidence, the translation of luteolin's promising preclinical data into clinical applications remains limited. The existing gap between laboratory findings and therapeutic utilization underscores the need for in-depth evaluation of its pharmacokinetics, bioavailability, and molecular targets in human subjects. Therefore, this review aims to elucidate the therapeutic promise of luteolin, focusing on its mechanisms of action and emerging strategies in the treatment of cancer and cardiovascular diseases. The objective is to rationalize the clinical relevance of luteolin as a novel adjunctive or standalone therapeutic agent and to encourage further translational research to validate its efficacy and safety in human populations.

THEMATIC DISCUSSION

Angina

Angina pectoris remains a major global health concern, characterized by transient episodes of thoracic discomfort arising from myocardial ischemia (6). Patients typically describe sensations of tightness, heaviness, or pressure localized to the chest, which may radiate to the shoulders, arms, or neck (7,8). The condition can be difficult to differentiate from other causes of chest pain such as gastroesophageal reflux disease, posing diagnostic challenges in clinical settings (9,10). Early recognition and timely medical evaluation are critical, as undiagnosed or poorly managed angina can progress to more serious cardiac events including myocardial infarction or sudden cardiac death (11,12). Epidemiological studies suggest that stable angina pectoris is associated with an annual incidence of myocardial infarction and death approaching 3–4%, underscoring the need for early therapeutic interventions (12). Current strategies—comprising lifestyle modifications, pharmacological management, and invasive procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)—have significantly improved outcomes and quality of life for affected individuals (13).

Pathophysiology of Angina

The underlying mechanism of angina pectoris involves a transient mismatch between myocardial oxygen supply and demand, culminating in ischemia (14). This imbalance may result from increased oxygen demand, such as during physical exertion, or reduced supply due to coronary obstruction or impaired perfusion (15). Atherosclerotic plaque formation is the most common cause, leading to luminal narrowing and compromised coronary flow reserve. However, not all patients with angina exhibit significant coronary artery stenosis. Some present with evidence of ischemia despite angiographically normal coronary arteries, implicating microvascular dysfunction or vasospasm as contributing factors (16). Acute coronary syndromes typically arise when an atherosclerotic plaque ruptures or erodes, initiating thrombus formation and abrupt cessation of blood flow (17). Preventive pharmacotherapy, including statins, ACE inhibitors, and antiplatelet agents, aims to stabilize plaques, reduce inflammation, and prevent myocardial infarction (18). Furthermore, antianginal medications such as nitrates, beta-blockers, and calcium channel blockers not only alleviate symptoms but also confer prognostic benefits in specific patient populations (19). Optimal management of chronic stable angina involves an integrated approach encompassing pharmacological therapy, lifestyle modification, and revascularization where indicated (20).

Prinzmetal Angina

Prinzmetal or variant angina represents a distinct clinical entity characterized by transient coronary vasospasm that often occurs at rest rather than during exertion (21). Unlike typical angina pectoris, which is precipitated by atherosclerotic obstruction, Prinzmetal angina arises from reversible constriction of the coronary arteries (9,21). The episodes are frequently nocturnal or early morning in occurrence and can manifest with transient ST-segment elevation on electrocardiography. Standard treatment strategies primarily aim at symptom relief and prevention of atherosclerotic progression (22). However, due to its vasospastic nature, the management of Prinzmetal angina necessitates specific therapies that target the reduction of coronary spasm and restoration of normal endothelial function (23). In this context, luteolin—a naturally occurring flavonoid—has attracted increasing attention for its vasodilatory and cardioprotective properties (24). By enhancing endothelial nitric oxide (NO) synthesis, luteolin contributes to vascular relaxation and may counteract coronary vasoconstriction, offering a potential complementary strategy in the treatment of ischemic angina (25,26).

Pathophysiology of Vasospastic Angina

Vasospastic angina (VSA) is primarily defined by abnormal coronary vasomotion, involving transient constriction of the epicardial arteries due to endothelial or smooth muscle dysfunction (27). This condition is multifactorial, with contributory roles from oxidative stress, genetic predisposition, and autonomic nervous system imbalance (18). Focal vasospasm arises from localized hyperreactivity of the vascular smooth muscle, whereas diffuse endothelial dysfunction can induce multivessel spasm (19). The pathophysiology also implicates vascular smooth muscle cell (VSMC) hypercontractility, which is mediated by aberrant calcium signaling and heightened sensitivity to vasoconstrictors (10). Dysregulation in nitric oxide, phospholipase C, and ATP-sensitive potassium (KATP) channels contributes to the exaggerated vasoconstrictive response characteristic of VSA (11–13). These molecular disruptions collectively precipitate ischemic episodes that are reversible yet potentially severe if unrecognized (14).

Dysfunction of Endothelium: The endothelium plays a vital role in regulating vascular tone through the synthesis of vasodilatory molecules such as nitric oxide (NO) (15). In a healthy state, NO inhibits platelet aggregation, suppresses vascular inflammation, and promotes relaxation of vascular smooth muscle cells. However, endothelial dysfunction—often precipitated by oxidative stress, hyperlipidemia, or smoking—reduces NO bioavailability and increases levels of vasoconstrictors such as angiotensin II and endothelin (16,17). In patients with vasospastic angina, this imbalance leads to paradoxical vasoconstriction in response to endothelium-dependent vasodilators like acetylcholine and histamine (17). Consequently, restoring endothelial health remains a primary therapeutic target, both to prevent vasospasm and to stabilize vascular function.

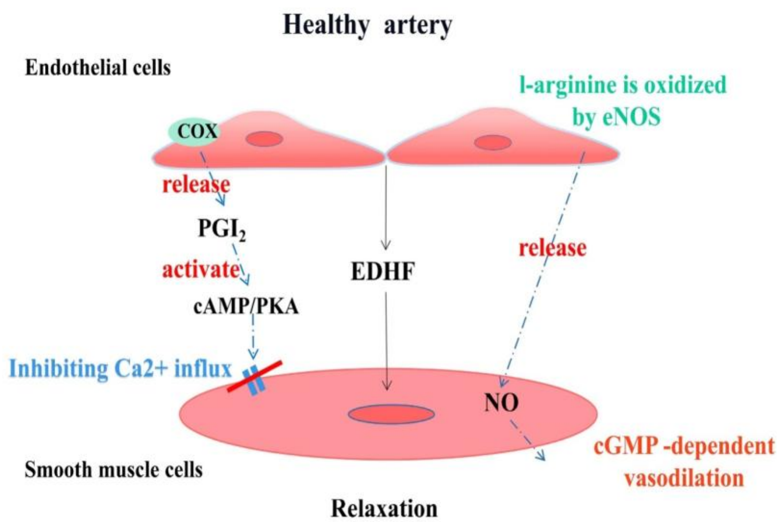
Chronic Inflammation: Chronic low-grade inflammation is increasingly recognized as a major contributor to vasospastic angina (18). Elevated levels of inflammatory biomarkers, including high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and adhesion molecules, have been consistently associated with endothelial dysfunction and vascular hyperreactivity (15). Studies have revealed inflammatory infiltrates within coronary adventitia and perivascular adipose tissue, particularly in smokers, indicating the localized nature of vascular inflammation (19,20). Persistent inflammation exacerbates oxidative stress, impairs NO signaling, and predisposes to recurrent vasospastic episodes. The inflammatory hypothesis of VSA thus reinforces the need for anti-inflammatory and antioxidant interventions alongside traditional vasodilatory therapy.

Clinical Spectrum

The clinical manifestations of vasospastic angina are diverse, typically involving non-exertional chest pain that responds rapidly to nitrates (8). Episodes most commonly occur at rest, often during nighttime or early morning hours, corresponding with variations in autonomic tone (18,21). In one cohort study at the Cleveland Clinic involving 59 patients, 93% presented with rest angina (21). Similarly, a study demonstrated through provocative testing that 38% of patients had rest angina alone, while smaller subsets exhibited both rest and exertional components (22). Severe episodes may present with diaphoresis, nausea, or syncope (10). Although most patients respond well to short-acting nitrates and calcium channel blockers (23), a minority exhibit refractory vasospasm despite optimal therapy (24,25). Spontaneous remission occurs in some individuals, though relapses are not uncommon (21,24). Silent ischemia remains a concern, as asymptomatic patients may still experience myocardial injury and atherosclerotic progression (26,27). Circadian variations in symptom onset are believed to relate to fluctuations in autonomic and hormonal activity, including catecholamines, cortisol, vasopressin, and inflammatory cytokines (18,19). A rare but noteworthy variant, Kounis syndrome—also known as "allergic angina"—combines coronary vasospasm with hypersensitivity reactions, necessitating prompt recognition and tailored treatment (10–12).

Mechanisms of Action of Luteolin

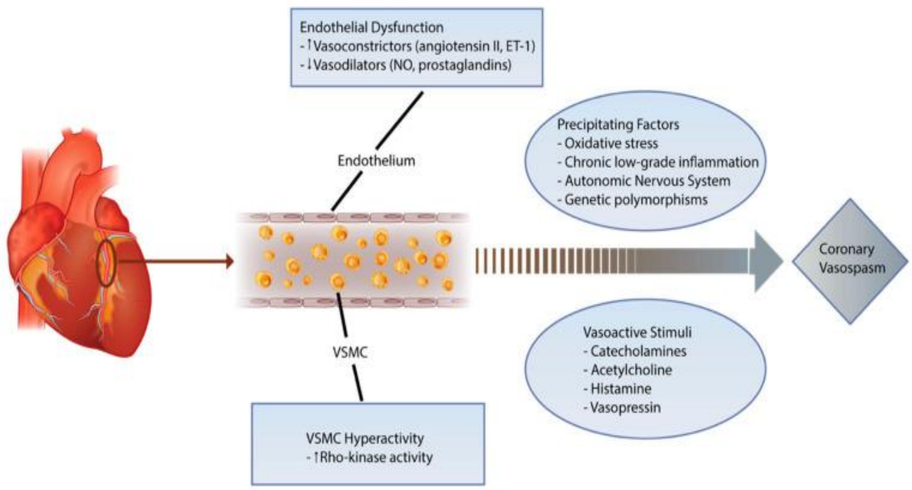
Luteolin exerts multiple cardioprotective effects through its antioxidant, anti-inflammatory, and vasodilatory properties. A key mechanism involves upregulation of endothelial nitric oxide synthase (eNOS), leading to increased production of NO—a critical mediator of vascular relaxation (23,24). Enhanced NO bioavailability alleviates coronary vasospasm, improves endothelial function, and promotes coronary blood flow (15). Simultaneously, luteolin mitigates oxidative stress by scavenging reactive oxygen species (ROS) and enhancing endogenous antioxidant enzymes such as superoxide dismutase and catalase (1,13). This antioxidant effect protects endothelial cells from oxidative damage and supports vascular integrity. Inflammatory suppression represents another vital pathway through which luteolin functions. It inhibits pro-inflammatory cytokines such as TNF-α and IL-6 and downregulates NF-κB activation, reducing vascular inflammation and subsequent vasoconstriction (16–18). Furthermore, luteolin modulates calcium homeostasis by regulating voltage-dependent calcium channels in vascular smooth muscle cells, thereby preventing excessive contraction and promoting vasodilation (19,23). Collectively, these mechanisms suggest that luteolin may serve as a promising adjunctive therapy for Prinzmetal angina by addressing both endothelial dysfunction and smooth muscle hyperreactivity. Its multifaceted pharmacological profile offers a foundation for future clinical studies exploring phytotherapeutic interventions in coronary vasospasm and ischemic heart disease.



Flavonoids Regulating Endothelial Function

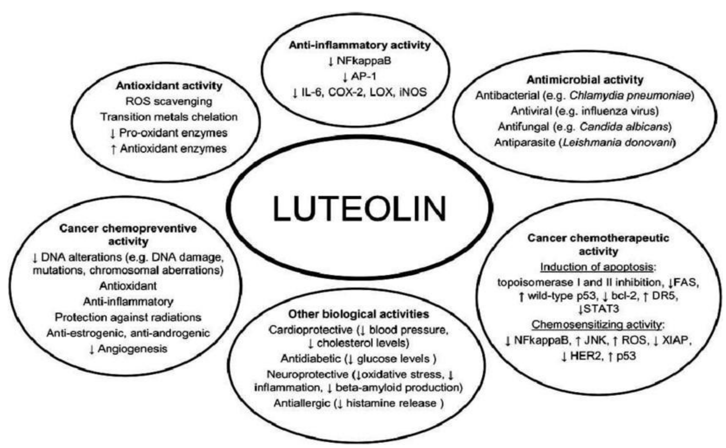
Figure 1 Flavonoids Regulation Endothelial Function

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION



Pathophysiology of Coronary Vasospasm

Figure 2 Pathophysiology of Coronary Vasospasm



Physiological Functions and Potential Modes of Action of Luteolin

Figure 3 Physiological Functions and Potential Modes of Action of Luteolin

CRITICAL ANALYSIS AND LIMITATIONS

The current body of evidence on vasospastic and exertional angina—and on luteolin as a putative adjunct—exhibits important methodological constraints that temper confidence in efficacy claims and limit translational readiness. Most studies synthesizing the pathobiology and clinical spectrum of vasospastic angina (VSA) are observational cohorts or narrative reviews with small samples and heterogeneous inclusion criteria, while rigorously designed randomized controlled trials (RCTs) remain scarce, particularly for pharmacologic strategies beyond calcium channel blockers and nitrates (e.g., adjunctive endothelial-targeted therapies) (1,2). Where

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

interventional data exist, follow-up is often short, curtailing the ability to assess hard outcomes such as myocardial infarction, malignant arrhythmias, or mortality, and leaving relapse dynamics or circadian clustering insufficiently characterized (11,13). Evidence specific to luteolin is even more preliminary: recent reports demonstrate anti-inflammatory, antioxidant, and endothelial-protective actions in cell and animal models, but controlled human cardiovascular trials are largely absent, and existing translational claims are extrapolated from preclinical or non-cardiac disease contexts with limited external validity (14–17). Methodological bias and confounding further complicate inference. Diagnostic non-uniformity persists across VSA studies—ergonovine versus acetylcholine provocation, differing thresholds for epicardial spasm, and variable incorporation of microvascular testing—which introduces selection bias by preferentially enrolling patients with readily provokable, more overt vasospasm while under-capturing microvascular phenotypes (1,2). Performance bias commonly arises from open-label designs and limited blinding in therapeutic comparisons; background therapies (e.g., statins, ACE inhibitors) that modulate endothelial function are unevenly reported or controlled, confounding estimated treatment effects (11,12). For luteolin, product heterogeneity (source plant, extraction methods, purity), unknown pharmacokinetic profiles in cardiac patients, and unmeasured dietary co-intake are frequent sources of bias; in vitro concentrations seldom map to achievable human exposures, and dose–response relationships remain undefined (4–7).

Publication bias likely inflates apparent benefits. Cohort and case-series literature on VSA is rich in positive or mechanistically compelling findings, whereas negative or equivocal provocation-test studies, and neutral adjunctive-therapy trials, are underrepresented in the published record (1,2). The phytochemical literature shows a similar skew: mechanistic reports highlighting suppression of NF-κB signaling, redox stress, or endothelial activation predominate, while null results, toxicity signals, or interaction studies with standard anti-anginals are seldom reported, raising concerns of selective reporting and citation amplification (4–7). Outcome heterogeneity also limits comparability. Across VSA studies, endpoints range from symptom diaries and nitrate responsiveness to ECG surrogates, provocation-test positivity, or composite “ischemic burden,” each with different sensitivity to circadian variation and autonomic tone (1,3). Hard clinical endpoints are rarely powered. In luteolin research, success is variously defined by reductions in inflammatory mediators, increases in endothelial nitric oxide bioactivity, or cellular permeability assays—useful mechanistic markers but only weakly linked to patient-centered outcomes without adjudicated clinical events or validated vascular function measures (e.g., acetylcholine flow reserve, coronary flow velocity reserve) (5–7). This variability complicates meta-analytic synthesis and inflates between-study heterogeneity.

Generalizability is another recurring weakness. Much of the contemporary VSA literature originates from single-center or regional cohorts with distinct environmental and pharmacogenomic profiles, particularly in East Asian populations where VSA prevalence and reactivity patterns differ from Western cohorts, limiting extrapolation to broader, multi-ethnic settings (12,13). Special populations—women, individuals with diabetes, chronic kidney disease, or multisystem allergic disease (relevant to Kounis syndrome)—are under-studied, despite biologically plausible differences in endothelial biology and vasomotor reactivity (3,9). Luteolin investigations rarely include patients with polypharmacy typical of coronary disease, leaving potential interactions with calcium channel blockers, long-acting nitrates, antiplatelets, and antihypertensives unknown (4–7). Collectively, these limitations justify a cautious interpretation of current findings and outline priorities for future work: adequately powered, multicenter RCTs that adopt standardized diagnostic criteria and core outcome sets for VSA; longer follow-up with adjudicated major adverse cardiac events; pre-registered translational trials of luteolin with quality-controlled preparations, pharmacokinetic–pharmacodynamic characterization, and interaction testing against guideline therapies; and deliberate recruitment of diverse populations to enhance external validity (1–7). Until such data are available, luteolin should be considered investigational in angina care, and conclusions about its additive benefit beyond established therapies should be framed as hypothesis-generating rather than definitive (7,9).

IMPLICATIONS AND FUTURE DIRECTIONS

The accumulated evidence from existing literature provides a valuable foundation for understanding the role of vasospastic mechanisms in angina and the emerging therapeutic promise of luteolin in cardiovascular pharmacology. Clinically, these findings underscore the potential for integrating flavonoid-based adjuncts such as luteolin into current management paradigms for vasospastic and Prinzmetal angina, particularly where conventional therapies like calcium channel blockers and nitrates achieve only partial control (1,2). Its antioxidant and endothelial-protective actions suggest that luteolin could complement standard pharmacological strategies by addressing oxidative stress, endothelial dysfunction, and inflammatory pathways that remain inadequately targeted in present regimens (3,4). This approach could improve vascular tone regulation, reduce recurrence of ischemic episodes, and enhance quality of life for patients with refractory vasospastic angina. However, until human clinical data become more robust, its use should remain experimental and carefully supervised within controlled investigational frameworks (5). From a policy and guideline perspective, the growing evidence base highlights an unmet need to incorporate endothelial and inflammatory modulation into clinical algorithms for angina management (12,16). Current guidelines largely emphasize anti-ischemic therapies focused on symptom control and coronary revascularization, with less consideration of vascular biology or nutraceutical interventions. If ongoing and future trials confirm the safety and efficacy of luteolin, evidence-based recommendations could evolve to include standardized phytochemical adjuncts as secondary preventive agents for specific patient subgroups. Regulatory and policy bodies would also need to define quality control, pharmacovigilance, and dosage standardization for botanical compounds like luteolin, which currently lack harmonized manufacturing or clinical use standards (17).

Despite encouraging laboratory data, multiple unanswered questions remain. The pharmacokinetics and bioavailability of luteolin in cardiac tissue are poorly understood, particularly regarding its metabolism, interaction with conventional anti-anginals, and capacity to achieve therapeutic plasma concentrations in humans (14,18). The specific mechanisms by which luteolin influences coronary vasospasm—beyond nitric oxide signaling—also require clarification, including potential modulation of calcium channels, endothelin pathways, and inflammatory transcription factors. Additionally, there is limited data on long-term cardiovascular safety and possible pro-oxidant effects at high concentrations or in polypharmacy settings (18,19). Research gaps also persist in understanding differential responses across populations with varying genetic backgrounds, comorbidities, and dietary exposures, especially given the ethnic and regional variation in vasospastic angina incidence (26).

Future research should prioritize well-powered, multicenter randomized controlled trials (RCTs) that incorporate standardized diagnostic criteria for vasospastic angina and uniform endpoints such as reduction in ischemic episodes, endothelial function metrics, and long-term major adverse cardiac events (19). Comparative trials evaluating luteolin against established endothelial modulators would provide critical insight into its clinical value. Pharmacokinetic–pharmacodynamic (PK–PD) studies are essential to determine optimal dosing, route of administration, and safety thresholds (24,25). Furthermore, longitudinal cohort studies integrating imaging and biomarker analyses could delineate whether chronic luteolin supplementation alters plaque stability or vascular remodeling. Advances in translational pharmacology, including nanocarrier-based delivery systems, may enhance bioavailability and enable controlled, targeted vascular release (5,10). In summary, the reviewed evidence positions luteolin as a promising but still exploratory therapeutic candidate in angina management. Clinicians should recognize its mechanistic plausibility while remaining cautious about premature clinical adoption. Future research integrating rigorous RCT design, standardized outcomes, and mechanistic biomarkers will be pivotal in determining whether luteolin can transition from a nutraceutical curiosity to a clinically validated cardioprotective agent. The insights gained may ultimately broaden therapeutic strategies, inspire novel guideline recommendations, and reinforce the growing recognition of phytochemicals in evidence-based cardiovascular care (26,27).

CONCLUSION

In conclusion, luteolin emerges as a promising natural therapeutic compound with significant potential in managing Prinzmetal angina through its multifaceted actions on endothelial function, nitric oxide synthesis, and vascular smooth muscle modulation. Evidence from preclinical and limited clinical studies suggests that luteolin enhances vasodilation, mitigates vasoconstrictive episodes, and improves overall vascular reactivity, thereby addressing key pathophysiological mechanisms underlying vasospastic angina. While these findings provide a compelling foundation, the current evidence remains preliminary and constrained by small sample sizes, heterogeneous methodologies, and limited clinical validation. Nonetheless, luteolin’s dual antioxidant and anti-inflammatory properties offer a valuable adjunctive approach, particularly for patients with suboptimal responses to conventional therapies. Future large-scale, well-designed clinical trials are essential to elucidate its pharmacokinetics, optimize dosing, and evaluate its integration within established treatment protocols. Strengthening this evidence base will determine whether luteolin can transition from experimental promise to a standardized therapeutic adjunct in contemporary angina management.

AUTHOR CONTRIBUTION

Author	Contribution
Sidra Sabir	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Ishrat Younus*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Tahmina Maqbool	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Farzana Sadaf	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

REFERENCES

1. Saleem H, Anwar S, Alafnan A, Ahemad N. Luteolin. A Centum of Valuable Plant Bioactives: Elsevier; 2021. p. 509-23.

2. Çetinkaya M, Baran Y. Therapeutic potential of luteolin on cancer. Vaccines. 2023;11(3):554.

3. Chen H-I, Hu W-S, Hung M-Y, Ou H-C, Huang S-H, Hsu P-T, et al. Protective effects of luteolin against oxidative stress and mitochondrial dysfunction in endothelial cells. Nutrition, Metabolism and Cardiovascular Diseases. 2020;30(6):1032-43.

4. Yao X, Zhou Z. Dietary intake of luteolin is negatively associated with all-cause and cardiovascular mortality in chronic kidney disease patients. BMC Public Health. 2024;24(1):2044.

5. Ford TJ, Berry C. Angina: contemporary diagnosis and management. Heart. 2020;106(5):387-98.

6. Manfredi R, Verdoia M, Compagnucci P, Barbarossa A, Stronati G, Casella M, et al. Angina in 2022: Current perspectives. Journal of clinical medicine. 2022;11(23):6891.

7. Osuman AK. The Importance of Clinical Examination of Patients with Dyspnea and Chest Pain in Choosing the Right Treatment Strategy: Lithuanian University of Health Sciences (Lithuania); 2024.

8. Rogers J, Collins G, Husain M, Docherty M. Identifying and managing functional cardiac symptoms. Clinical Medicine. 2021;21(1):37-43.

9. Joshi PH, De Lemos JA. Diagnosis and management of stable angina: a review. Jama. 2021;325(17):1765-78.

10. Chhabra J, Mubder M, Tak N, Houshmand N, Siddiqui A, Cyrus T, et al. Life after Coronary Artery Bypass Grafting: Lifestyle Changes, Secondary Prevention, and Quality of Life. International Journal of Angiology. 2025.

11. Heusch G. Myocardial ischemia/reperfusion: translational pathophysiology of ischemic heart disease. Med. 2024;5(1):10-31.

12. Lanza O. Linking platelet reactivity, cardiac autonomic dysfunction and inflammation in patients with acute coronary syndromes: a complex puzzle to be solved with potential therapeutic implications. 2025.

13. Kunadian V, Chieffo A, Camici PG, Berry C, Escaned J, Maas AH, et al. An EAPCI expert consensus document on ischaemia with non-obstructive coronary arteries in collaboration with European Society of Cardiology Working Group on Coronary

Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. European heart journal. 2020;41(37):3504-20.

14. Fahed AC, Jang I-K. Plaque erosion and acute coronary syndromes: phenotype, molecular characteristics and future directions. Nature Reviews Cardiology. 2021;18(10):724-34.

15. Mir MA, Dar MA, Qadir A. Exploring the Landscape of Coronary Artery Disease: A Comprehensive Review. Am J Biomed Pharm. 2024;1:9-22.

16. Knuuti J, Wijns W, Funck-Brentano C. Anti-ischaemic medication must be adapted to each patient's characteristics and preferences in patients with chronic coronary syndromes. European Heart Journal. 2020;41(3):480-1.

17. Montone RA, Rinaldi R, Niccoli G, Andò G, Gragnano F, Piccolo R, et al. Optimizing management of stable angina: a patient-centered approach integrating revascularization, medical therapy, and lifestyle interventions. Journal of the American College of Cardiology. 2024;84(8):744-60.

18. Nguyen TH, Ong G-J, Girolamo OC, De Menezes Caceres' V, Muminovic A, Chirkov YY, et al. Angina due to coronary artery spasm (variant angina): Diagnosis and intervention strategies. Expert review of cardiovascular therapy. 2021;19(10):917-27.

19. Jenkins K, Pompei G, Ganzorig N, Brown S, Beltrame J, Kunadian V. Vasospastic angina: a review on diagnostic approach and management. Therapeutic advances in cardiovascular disease. 2024;18:17539447241230400.

20. Beltrame JF. Management of vasospastic angina. Heart. 2023;109(1):70-7.

21. Dong M, Luo Y, Lan Y, He Q, Xu L, Pei Z. Luteolin reduces cardiac damage caused by hyperlipidemia in Sprague-Dawley rats. Heliyon. 2023;9(6).

22. Yang W, Li Q, Duncan JW, Bakrania BA, Bradshaw JL, Granger JP, et al. Luteolin-induced vasorelaxation in uterine arteries from normal pregnant rats. Pregnancy hypertension. 2021;23:11-7.

23. Tang F, Yan H-L, Wang L-X, Xu J-F, Peng C, Ao H, et al. Review of natural resources with vasodilation: traditional medicinal plants, natural products, and their mechanism and clinical efficacy. Frontiers in pharmacology. 2021;12:627458.

24. Rehan R, Weaver J, Yong A. Coronary vasospastic angina: a review of the pathogenesis, diagnosis, and management. Life. 2022;12(8):1124.

25. Liu S, Lin Z. Vascular smooth muscle cells mechanosensitive regulators and vascular remodeling. Journal of Vascular Research. 2022;59(2):90-113.

26. Dai C, Khalil RA. Calcium Signaling Dynamics in Vascular Cells and Their Dysregulation in Vascular Disease. Biomolecules. 2025;15(6):892.

27. Yu L, Lu X, Xu C, Li T, Wang Y, Liu A, et al. Overview of microvascular angina pectoris and discussion of traditional Chinese medicine intervention. Evidence-Based Complementary and Alternative Medicine. 2022;2022(1):1497722.

