Acta Pharmaceutica Sinica B 2026;16(3):1797−1799

Chinese Pharmaceutical Association
Institute of Materia Medica, Chinese Academy of Medical Sciences

Acta Pharmaceutica Sinica B

www.elsevier.com/locate/apsb
www.sciencedirect.com

COMMENTARY

Integrating Chinese medicine and intermittent fasting: A promising approach for treating diabetic vascular calcification

KEY WORDS

Chinese medicine;
Intermittent fasting;
Diabetic vascular calcification

Vascular calcification (VC) is a major cause of cardiovascular disease morbidity and mortality in diabetic patients, and it is one of the core pathological features of diabetes-induced vascular damage and remodeling[1]. Although several mechanisms, such as oxidative stress and inflammation, have been proposed to play a role in the occurrence and development of VC, and treatment strategies targeting these underlying factors have been developed, the effectiveness of these therapies remains limited and faces many challenges. To date, effective prevention and treatment of VC remains an unmet clinical need. In the latest article in *APSB*[2], a team led by Yue Liu explored an innovative approach combining traditional Chinese medicine (TCM) with intermittent fasting (IF) to treat diabetic vascular calcification (DVC). The authors validated the significant effects of Chinese medicine and intermittent fasting integration therapy (CMIT) in the treatment of DVC through *in vivo* and *in vitro* models. They found that this therapy effectively alleviates VC by inhibiting the osteogenic differentiation of vascular smooth muscle cells (VSMC). This study not only reveals the potential mechanisms behind the combination of Chinese medicine and dietary intervention but also provides new insights into the treatment of DVC.

1. The complex mechanism of diabetic vascular calcification

The characteristic of VC is the accumulation of calcium phosphate crystals, accompanied by the local expression and deposition of regulatory mineralization proteins. This process can occur in the intimal and medial layers of blood vessels. Although hydroxyapatite deposition is a common hallmark of various types of VC, the initiating factors, molecular pathways of diffusion, and even the crystal composition of calcium phosphate may differ in VC induced by different diseases. In diabetes, calcification begins in the vascular media and eventually leads to concentric thickening of the vessel wall. Hyperglycemia and dysregulated calcium-phosphate metabolism are the initiating factors for VC[3]. The combined effects of both gradually disrupt vascular redox homeostasis, exacerbating endothelial dysfunction, triggering inflammatory signaling cascades, oxidative stress, and cell apoptosis, all of which drive VSMC to undergo active osteoblastic phenotype transformation, inducing osteogenic remodeling of blood vessels. Specifically, under high-glucose conditions, changes occur in glucose metabolism pathways such as hexosamine, polyols, pentose phosphate, and glycolysis. Reactive oxygen species accumulate continuously in the blood vessels, activating multiple cellular pathways such as AGE/RAGE, NF-κB, Wnt/β-catenin, and others, leading to endothelial cell dysfunction. Damaged endothelial cells synthesize and secrete a large number of inflammatory mediators, which promote the expression of osteogenic transcription factors in VSMCs, such as Runx2, BMP2 and osteopontin, driving their osteogenic transformation. Additionally, hyperglycemia exacerbates intracellular calcium−phosphate balance, promoting calcium activation and

Peer review under the responsibility of Chinese Pharmaceutical Association and Institute of Materia Medica, Chinese Academy of Medical Sciences.

https://doi.org/10.1016/j.apsb.2026.01.004

endoplasmic reticulum stress, which increases *O*-GlcNAc glycosylation and facilitates the deposition of hydroxyapatite in the vascular wall.

In recent years, many studies have focused on exploring the effects of anti-diabetic drugs or phosphate binders on DVC, including SGLT2 inhibitors, metformin, and glucagon-like peptide-1 receptor[4]. Interestingly, these studies do not primarily regard glucose-lowering as the main mechanism for treating DVC, but instead extend the focus to multiple molecular mechanisms beyond glucose reduction, such as anti-inflammatory, anti-oxidative stress, and improvement of endothelial cell dysfunction. The exploration of drugs with comprehensive regulatory effects and the further development of multi-target, systematic, and integrated intervention strategies have become an increasingly prominent trend in the treatment of metabolic vascular diseases.

2. The modern integration of traditional Chinese medicine and dietary patterns: A new paradigm for clinical management of diabetic vascular calcification

Given the widespread use of polypharmacy among diabetes patients, non-pharmacological therapies, such as dietary modifications, have garnered increasing attention as strategies to combat metabolic cardiovascular diseases. Compared to other dietary patterns such as calorie restriction and the Mediterranean diet, IF, which limits the eating window to just a few hours each day, is more easily accepted and has been shown to preserve key metabolic and cardiovascular benefits[5]. However, recent studies have raised some concerns about this popular dietary approach. Matta et al.[6] found that IF has an age-dependent effect on glucose metabolism, particularly on pancreatic β-cell function. Short-term IF can improve glucose homeostasis and insulin sensitivity, while long-term IF's impact on β-cells is constrained by age. Other studies have shown that the metabolic improvements associated with IF may have a "available period", with prolonged, solely IF-based interventions potentially leading to resistance or even reduced efficacy[7]. Moreover, despite repeated validation of its benefits in animal studies, the practical application of IF in diabetes populations faces significant challenges due to adherence issues and individual variability. As a result, these dietary trends are difficult to translate directly into implementable, scalable treatment plans. An integrated strategy combining multiple modes of intervention is gradually emerging as a new direction in the clinical management of metabolic vascular diseases.

In recent years, the effectiveness and potential of TCM in the prevention and treatment of metabolic cardiovascular diseases have garnered global attention. In their latest study, Yue Liu's team pioneered the CMIT strategy by combining their previously developed anti-DVC formula, DanLian-TongMai (DLTM)[8], with a time-restricted feeding approach[2]. They found that the integrated treatment of DLTM with IF significantly outperformed either the Chinese medicine or dietary intervention alone in improving calcium-phosphate metabolic disorders, reducing aortic calcification, and inhibiting VSMC osteoblastic transformation in mice, demonstrating a synergistic effect in combating DVC. Additionally, the team used ultra-high-performance liquid chromatography−mass spectrometry (UHPLC−MS) to track the prototype compounds of DLTM and identified eight core anti-calcification components. *In vitro* experiments further confirmed that the combined effect of intermittent serum deprivation (simulating IF) and the core anti-calcification components of DLTM effectively inhibited VSMC proliferation and reduced cellular calcium content. This suggests that CMIT not only has superior efficacy in improving DVC but also demonstrates significant synergistic effects, providing a practical and feasible new paradigm for the clinical management of DVC.

3. Tpm1 as a potential drug target for diabetic vascular calcification

How metabolic changes induce gene expression and vascular cell phenotype reprogramming is currently a focal point in the study of metabolic vascular diseases. Wang et al.[2] investigated the mechanism of action of CMIT through transcriptome sequencing. They found that tropomyosin 1 (Tpm1) is involved in the formation and progression of DVC. Rats with *Tpm1* knockdown exhibited a more severe VC phenotype and reversed the anti-calcification effects of CMIT. TPM1, as an actin-binding protein, regulates biological structure and function by modulating muscle contraction and the formation and maintenance of the cytoskeleton, thus performing essential roles in structural support and signal transduction. Previous studies have reported that Tpm1 regulates the dynamics and functions of actin filaments in the cytoskeleton, inhibiting VSMC proliferation and migration. Moreover, Tpm1 mediates the calcium response of the actin filaments in both skeletal and cardiac muscle through the troponin complex, suggesting a protective role in VC[9]. The authors also found that Tpm1 co-localizes with stress fibers and smooth muscle actin (αSMA), and its downregulation leads to changes in the cellular phenotype. Further bioinformatics analysis revealed that Tpm1's action in VSMC is driven by the upstream microRNA miR21-5p. Tpm1 participates in miR21-5p-regulated VSMC osteoblastic transformation and arterial calcification. A recent study also found that targeting Tpm1-mediated cytoskeletal remodeling effectively inhibits VSMC proliferation, migration, and phenotype transformation, thus alleviating vascular remodeling and intimal thickening (Fig. 1)[10].

Finally, the biological mechanism by which CMIT influences Tpm1 in regulating VSMC osteoblastic transformation remains unclear. Given that VSMC osteoblastic transformation is also influenced by osteogenic genes such as Runx2, BMP2, OPN, etc., studies have shown that CMIT inhibits the expression of osteogenic proteins like Runx2 and BMP2. Therefore, the anti-calcification benefits of CMIT may not be simply explained by stabilizing the actin filaments of the cytoskeleton. In addition, besides time-restricted feeding, it remains to be explored whether other forms of IF, such as alternate-day fasting or the 5:2 diet, can produce similar effects. Furthermore, it is worth investigating whether the anti-calcification effects of time-restricted feeding are consistent across different time windows. These questions warrant further research. While many questions remain to be addressed, Yue Liu's study successfully integrates the wisdom of traditional Chinese medicine with modern nutritional theory, offering an innovative solution for the clinical management of DVC[2].

In conclusion, the integrated approach of combining Chinese medicine with dietary interventions, as proposed by Wang et al.[2], establishes a compelling new paradigm for addressing metabolic vascular diseases. Notably, given that VC associated with diabetes and chronic kidney disease (CKD) shares pathophysiological similarities—such as medial calcification being the predominant calcification phenotype in both conditions, CMIT may also hold potential therapeutic value and clinical benefits in preventing or

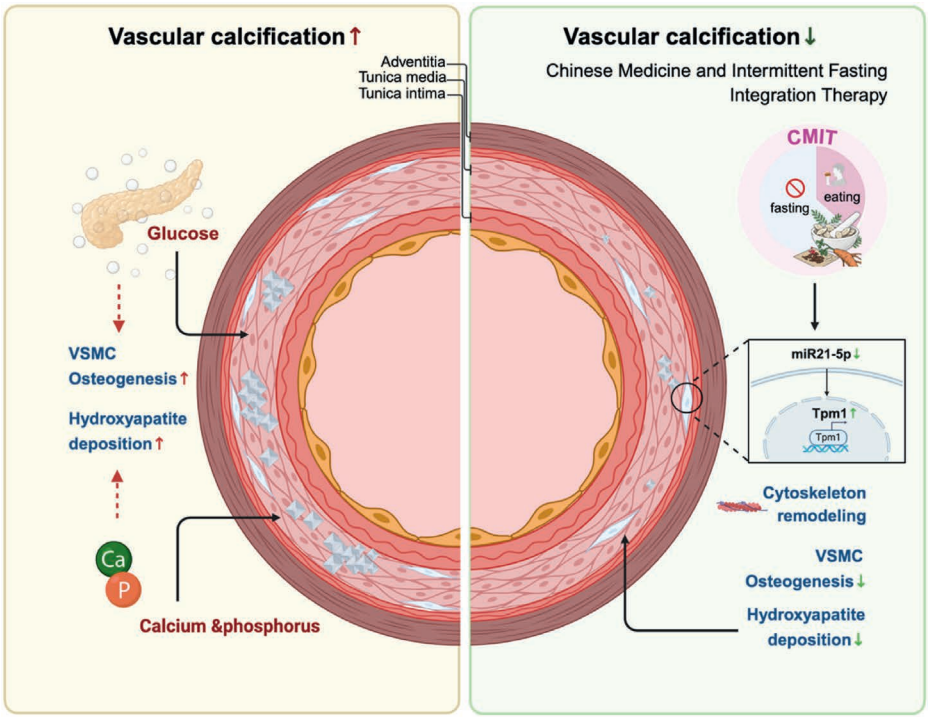

Figure 1 Effect of CMIT on VC in diabetes mellitus. Under diabetic conditions, elevated glucose levels promote VSMC osteogenic differentiation and hydroxyapatite deposition. CMIT attenuates VC by stabilizing the VSMC cytoskeleton through modulation of the miR21-5p/Tpm1 pathway, thereby inhibiting osteogenic differentiation. VSMC, vascular smooth cell; CMIT, Chinese medicine and intermittent fasting integration therapy. ↑ increase; ↓ decrease.

attenuating CKD-related VC, warranting further systematic investigation. Collectively, this strategy opens new avenues for future research and holds promise for advancing the clinical prevention and treatment of these complex metabolic vascular disorders.

References

1. Yao H, Sun Z, Zang G, Zhang L, Hou L, Shao C, et al. Epidemiological research advances in vascular calcification in diabetes. *J Diabetes Res* 2021;**2021**:4461311.
2. Wang W, Liu Y, Li Y, Xu Q, Zhu M, Cui J, et al. Chinese medicine and intermittent fasting integration therapy attenuate diabetic vascular calcification *via* miR21-5p/Tpm1-mediated osteogenic differentiation of VSMCs. *Acta Pharm Sin B* 2026;**16**:352−70.
3. Flores-Roco A, Lago BM, Villa-Bellosta R. Elevated glucose levels increase vascular calcification risk by disrupting extracellular pyrophosphate metabolism. *Cardiovasc Diabetol* 2024;**23**:405.
4. Ghosh S, Luo D, He W, Chen J, Su X, Huang H. Diabetes and calcification: the potential role of anti-diabetic drugs on vascular calcification regression. *Pharmacol Res* 2020;**158**:104861.
5. Zhang J, Chen Y, Zhong Y, Wang Y, Huang H, Xu W, et al. Intermittent fasting and cardiovascular health: a circadian rhythm-based approach. *Sci Bull (Beijing)* 2025;**70**:2377−89.
6. Matta L, Weber P, Erener S, Walth-Hummel A, Hass D, Bühler LK, et al. Chronic intermittent fasting impairs β cell maturation and function in adolescent mice. *Cell Rep* 2025;**44**:115225.
7. Wang Y, Feng C, Yu B, Wang J, Chen W, Song C, et al. Enhanced effects of intermittent fasting by magnetic fields in severe diabetes. *Research (Wash D C)* 2024;**7**:468.
8. Wang W, Li Y, Zhu M, Xu Q, Cui J, Liu Y, et al. Danlian-Tongmai formula improves diabetic vascular calcification by regulating CCN3/NOTCH signal axis to inhibit inflammatory reaction. *Front Pharmacol* 2025;**15**:1510030.
9. Reindl T, Giese S, Greve JN, Reinke PY, Chizhov I, Latham SL, et al. Distinct actin-tropomyosin cofilament populations drive the functional diversification of cytoskeletal myosin motor complexes. *iScience* 2022;**25**:104484.
10. Li S, Chen K, Zhang Y, Yu Y, Zhang T, Jiang D, et al. TSPAN4 controls vascular smooth muscle cell phenotypic switching and intimal hyperplasia by targeting TPM1-regulated cytoskeletal organization. *Clin Sci (Lond)* 2025;**139**:1145−61.

Zhixiu Lin
School of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong, China
E-mail address: linzx@cuhk.edu.hk

Received 29 November 2025
Received in revised form 17 December 2025
Accepted 4 January 2026