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Vitamin B6 attenuates aortic dissection by inhibiting pathological remodeling of the aortic extracellular matrix

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Abstract: **Background**: Aortic dissection (AD) is a serious medical condition characterized by a tear in the inner lining of the aorta that can lead to life-threatening complications and carries a high mortality rate. Vitamin B6 (B6) is a vital micronutrient required to maintain normal physiological function and has been reported to protect against various vascular diseases. However, its effects on AD remain insufficiently characterized. **Objective**: To investigate the potential therapeutic effects and mechanisms of B6 in a β-aminopropionitrile (BAPN)-induced mouse model of AD. **Methods**: A BAPN-induced AD model was established in 3-week-old C57BL/6J mice. B6 (50 mg/kg/day) was administered for four weeks, and body weight and mortality were recorded daily. Gross anatomical examination and histological staining were used to evaluate aortic morphology and elastin integrity. Western blotting and immunofluorescence were performed to assess changes in extracellular matrix (ECM) components in vivo and in vitro. Superoxide dismutase (SOD) activity and malondialdehyde (MDA) levels were measured as indicators of oxidative stress. **Results**: B6 supplementation significantly attenuated AD, as evidenced by reduced AD incidence, improved survival, preservation of aortic architecture, and decreased elastin degradation. B6 also exerted antioxidant effects, alleviating oxidative stress, which was associated with inhibition of smooth muscle cell phenotypic switching and reduced ECM degradation. **Conclusion**: B6 treatment may slow AD progression by protecting the aortic ECM from pathological remodeling through its antioxidant effects. These findings suggest that B6 supplementation may represent a promising therapeutic strategy for the prevention and treatment of AD.

Keywords: Aortic dissection; Extracellular matrix remodeling; Vitamin B6

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INTRODUCTION

Aortic dissection (AD) is a critical cardiovascular condition associated with high mortality and morbidity (Y. Zhou *et al*., 2024). The aortic wall is composed of three layers: the intima, media, and adventitia. AD initiates with a tear in the intimal layer, allowing blood to enter the medial layer, resulting in separation between the intima and adventitia and formation of true and false lumens (Nienaber *et al*., 2016). Timely intervention is essential to prevent fatal aortic rupture (Z. Zhou *et al*., 2022). Currently, treatment relies mainly on surgical approaches, with limited pharmacological options available, highlighting the need for novel therapeutic targets (Pape *et al*., 2015; Zhu *et al*., 2020).

The pathogenesis of AD remains incompletely understood, but the central role of extracellular matrix (ECM) disruption is well recognized (Shen *et al*., 2020). The ECM provides structural support and regulates aortic wall elasticity (Chakraborty *et al*., 2019). An imbalance in ECM homeostasis—whether due to deficiency or excess—can compromise aortic integrity, increasing susceptibility to dissection (Wu *et al*., 2013). Thus, maintaining ECM stability represents a promising therapeutic strategy. Apoptosis of vascular smooth muscle cells (VSMCs) and ECM degradation are key features of medial layer weakening. VSMCs are essential for synthesizing and organizing ECM components, and their ability to switch between contractile and synthetic phenotypes in response to stress is crucial for vascular adaptation.

Oxidative stress has been implicated in promoting VSMC phenotypic switching toward a synthetic state, accompanied by altered morphology, increased proliferation, and elevated secretion of proteolytic enzymes that degrade ECM, contributing to AD progression (Emeto *et al*., 2016; Kazaleh *et al*., 2023; Rombouts *et al*., 2022). It should be noted, however, that the mechanistic evidence linking oxidative stress to AD is still evolving, with certain aspects awaiting full consensus and alternative pathways under investigation.

Despite evidence supporting the role of micronutrients and antioxidants in vascular diseases, no prior studies have investigated the role of vitamin B6 in aortic dissection, despite the established relevance of ECM integrity and oxidative stress in its pathogenesis.

MATERIALS AND METHODS

Mouse aortic dissection model and dosing regimen

Wild-type male C57BL/6 mice were acquired from GemPharmatech Co. Ltd. The AD model was established using BAPN, purchased from Macklin (Shanghai, China) (Ren *et al*., 2016). C57BL/6 male mice (3 weeks old, weighing 7-8 g) were fed a regular diet. The sample size was selected based on the results of previous experiments and the experimental strategy. Sixty experimental mice

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were used in the aortic dissection experiment and randomly assigned to three groups, each containing 20 mice. The control group received 0.1 ml of physiological saline (0.9% sodium chloride) by gavage. The BAPN group received 0.1 ml of gavage BAPN (1 g/kg/day) in physiological saline. BAPN+B6 mice got 0.1 ml of BAPN and B6 (gavage, 50 mg/kg/day diluted in physiological saline). All experimental mice were diagnosed as AD according to the following criteria: autopsy revealed aortic wall rupture with blood infiltration, leading to the separation of aortic wall layers and the creation of a false lumen or a thrombus.

Survival rates, incidence of aortic dissection and body weights of mice

weight was assessed weekly for all the mice. Throughout the experimental duration, the survival status of the animals, the time of death, and the reason for death were documented. All the mice were anesthetized with 1% isoflurane at the end of the experiment (day 28). The mice were anesthetized, and the thoracic cavity was opened by careful dissection. Subsequent to the excision of the surrounding tissues under sterile conditions, the excised aortas were thoroughly rinsed multiple times with sterile saline to eliminate any leftover blood. Aortic tissues were collected for later research.

Histopathological analysis

Mouse aorta tissue samples were fixed with 4% paraformaldehyde for 48 h at room temperature (23-25°C), dried, embedded in paraffin, sectioned into 4 μm slices, and stained with Elastic Van Gieson (EVG) and Hematoxylin and Eosin (HE). The tissue morphology was ascertained by HE staining. Elastic EVG staining was used to assess the integrity of the aortic wall elastin. The elastin degradation classifications were based on the elastin degradation score, as follows: grade I, elastic laminae that were complete and well organized; grade II, elastic laminae with some fractures and interruptions; grade III, significant elastic laminae degradation and visible rupture sites; and grade IV, substantial elastin degradation and tear-out was evident. All histological analyses were performed at room temperature using a Microsystem instrument (Olympus IX73, Japan).

Determination of plasma superoxide dismutase activity and malondialdehyde levels

Blood samples were centrifuged using a H1650-W (Xiang Yi, China) at 3000 *g* for 20 minutes, after which the supernatant was collected and stored at -80 °C until the commencement of the tests. The activity of plasma superoxide dismutase (SOD) was assessed using a SOD assay kit (Solarbio, Beijing, China) according to the manufacturer's guidelines. Following the measurement of absorbance at 560 nm (Zhang *et al*., 2020), the protein concentration of the supernatant was determined in units per milliliter. Plasma malondialdehyde (MDA) concentrations were quantified using an MDA test kit (Solarbio, Beijing, China) according to the manufacturer's guidelines. The absorbance of the supernatant was measured at 450 nm (Ren *et al*., 2025) and reported in nmol per ml of protein.

Immunofluorescence

Prepared sections were incubated using a ZWY-240 (ZhiCheng, China) with 10% goat serum for one hour at 37° C. Membranes were incubated overnight at 4 °C with the primary antibody. The principal antibodies employed were α-smooth muscle actin (α-SMA) (1:100 dilution, Ab124964, Abcam) and smooth muscle 22 alpha (SM22α) (1:100 dilution, 10493-1-AP, Proteintech). Following washing, a secondary antibody labeled with fluorescein (Servicebio, Wuhan, China) was applied and incubated for 1 h at room temperature. The nuclear staining was done using 4′,6-diamidino-2-phenylindole (DAPI) (Servicebio, Wuhan, China). A digital slide scanner (Olympus VS200, Japan) was used to picture the sections. The fluorescence intensity was quantified using the ImageJ software.

Western blot

Radioimmunoprecipitation assay (RIPA) lysis buffer (Servicebio, Wuhan, China) containing protease inhibitors was used to extract proteins from aortic tissues. The bicinchoninic acid (BCA) method (Yang *et al*., 2025) (Servicebio, Wuhan, China) was used to measure the protein concentration. The protein was then denatured for 10 minutes at 100°C in a metal bath. The target protein was electrophoresed on 10% or 12.5% SDS-PAGE gels according to molecular weights and then transferred onto a polyvinylidene fluoride (PVDF) membrane (Servicebio, Wuhan, China). The membrane was blocked with 5% skim milk, incubated with the primary antibody for the entire night at 4°C, and then incubated with a secondary antibody conjugated with horseradish peroxidase for 2h at room temperature. The ECL reagent (Servicebio, Wuhan, China) was used for blot production, and ImageJ software was used for band analysis.

Statistical analysis

GraphPad Prism version 9.0 (GraphPad Prism Software, CA, USA) was used to analyze the data. The mean ± standard error of the mean is the way that data are expressed. One-way analysis of variance (ANOVA) and Bonferroni post-hoc analysis were used for comparisons. Statistical significance was defined as $P < 0.05$.

RESULTS

Following BAPN induction, Vitamin B6 reduced the incidence of Aortic dissection, enhanced mouse survival, enhanced aortic morphology, and prevented aortic dilatation. While B6 treatment decreased the incidence of AD to 40% (8/20), the incidence of AD was 80% (16/20) during the four weeks of BAPN administration, as shown in fig. 1. By the 4th experimental week, the control group had gained significant weight. Compared to the control

group, the BAPN group lost significantly more weight (Fig. 1B). Following the delivery of BAPN, B6 therapy enhanced the survival rate (30% vs. 80%) (Fig. 1C). Furthermore, when BAPN was administered, the maximal internal diameter of the thoracic aorta rose considerably compared to the control group. In BAPN-treated mice, B6 dramatically decreased aortic dilatation and enhanced aortic morphology (Figs. 1D and 1E).

Vitamin B6 impaired elastin degradation and inhibited false lumen formation after BAPN administration

The HE and EVG were performed to assess the histological features of AD. (Figs. 2A and 2B) show representative HE-stained and EVG-stained images of the mouse thoracic aorta following BAPN induction. Histological examination revealed false lumen formation, media destruction, and marked thickening of adventitia in the BAPN group. However, these alterations were markedly diminished by B6 therapy. The elastin scores of experimental mice were considerably enhanced following BAPN treatment. Furthermore, B6 treatment alleviated the rupture of elastic fibers (Fig. 2C).

Vitamin B6 inhibited oxidative stress

To evaluate the potential pathophysiological role of oxidative stress in AD, we assessed MDA levels and SOD activity. In comparison to the control group, the activity of the antioxidant enzyme SOD in the plasma of the BAPN group diminished, while the concentration of the oxidative stress marker MDA escalated. B6 therapy decreased MDA levels and enhanced SOD activity in the BAPN-treated mice (Figs. 3A and 3B).

Vitamin B6 inhibits aortic extracellular matrix degradation

Elastic and collagen fibers, vital constituents of the extracellular matrix, are crucial for the development and structural integrity of the vascular wall. ECM degradation leads to aortic dissection and aneurysm formation. To elucidate the pathogenic mechanism via which B6 mitigates the risk of Alzheimer's disease formation, we evaluated and quantified the deposition of collagen types I (COL-I) and III (COL-III) in aortic lesions via Western blot (WB) analysis. The findings demonstrated that the density of COL-I and COL-III in the B6-treated group was markedly reduced compared to the BAPN group at 28 days post-modeling (Figs. 4A-C).

Vitamin B6 ameliorates phenotypic switch and down-regulate MMPs expression in BAPN-induced VSMC

Immunofluorescence (IF) staining was conducted on the thoracic aortic sections to detect the contraction markers α-SMA and SM22α. BAPN markedly decreased α-SMA and SM22α levels, which were normalized after B6 treatment. Furthermore, WB analysis revealed that the treated group's α-SMA and SM22α levels had dropped, but that the B6 treatment had brought them back to normal (Figs. 5A-C). WB analysis was also used to detect matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) levels in the aorta. The MMP-2 and MMP-9 expression levels were significantly lower in the aortic tissues of B6- and BAPN-treated mice than in those of the BAPN-treated mice. The results obtained indicate that B6 stimulates VSMC differentiation signaling to inhibit aortic degeneration (Figs. 5D-G).

DISCUSSION

B6 is involved in numerous metabolic processes, including amino acid, fat and glucose metabolism (di Salvo, Contestabile, and Safo, 2011). Over the past decade, a growing number of studies have linked B6 to chronic diseases, particularly metabolic disorders such as diabetes and atherosclerosis. However, the effects of B6 on AD remain unclear (Friso, Lotto, Corrocher, and Choi, 2012; Mascolo and Vernì, 2020). This study presents evidence of the inhibitory role of B6 in the progression of AD. Our results indicate that B6 significantly enhances survival in AD-afflicted mice, reduces the incidence of AD and is associated with diminished aortic dilation and improved aortic structure. These findings suggest the potential of B6 as an innovative treatment approach for Aortic Dissection in mice.

Aortic dissection is partly characterized by abnormalities in ECM (Wu, Shen, Russell, Coselli, and LeMaire, 2013). Elastin and collagen, which are key components of the ECM in the aortic wall, play crucial roles in regulating mechanical function. Abnormalities in these components can lead to aortic dissection (Nakashima, Shiokawa, and Sueishi, 1990; Watanabe and Sawai, 1999). In this study, the beneficial effects of B6 treatment were attributed to its role in modulating ECM remodeling, which is essential for maintaining the structural integrity of the aortic wall. By impeding collagen deposition and averting elastin degradation, B6 seems to counteract ECM disruptions that cause aortic dissection. This implies that B6 may serve as an effective therapeutic agent for preventing or treating AD by reinstating the balance between the ECM composition and function.

Elevated oxidative stress adversely affects the vascular system, potentially leading to cardiovascular diseases (Emeto, Moxon, Au, and Golledge, 2016). Oxidative stress-induced inflammation of the arterial wall is a critical factor in pathological remodeling. SOD is an essential antioxidant enzyme (Strobel, Fassett, Marsh, and Coombes, 2011). SOD facilitates the transformation of superoxide anions into hydrogen peroxide (H2O2) and molecular oxygen (O2) (Faraci and Didion, 2004). Lipid peroxidation's result, MDA, is a recognized indicator of oxidative stress. Previous studies have shown that oxidative stress contributes to vascular damage and is involved in AD pathogenesis (Prasad, McNair, Qureshi, and Casper-Bell, 2012).

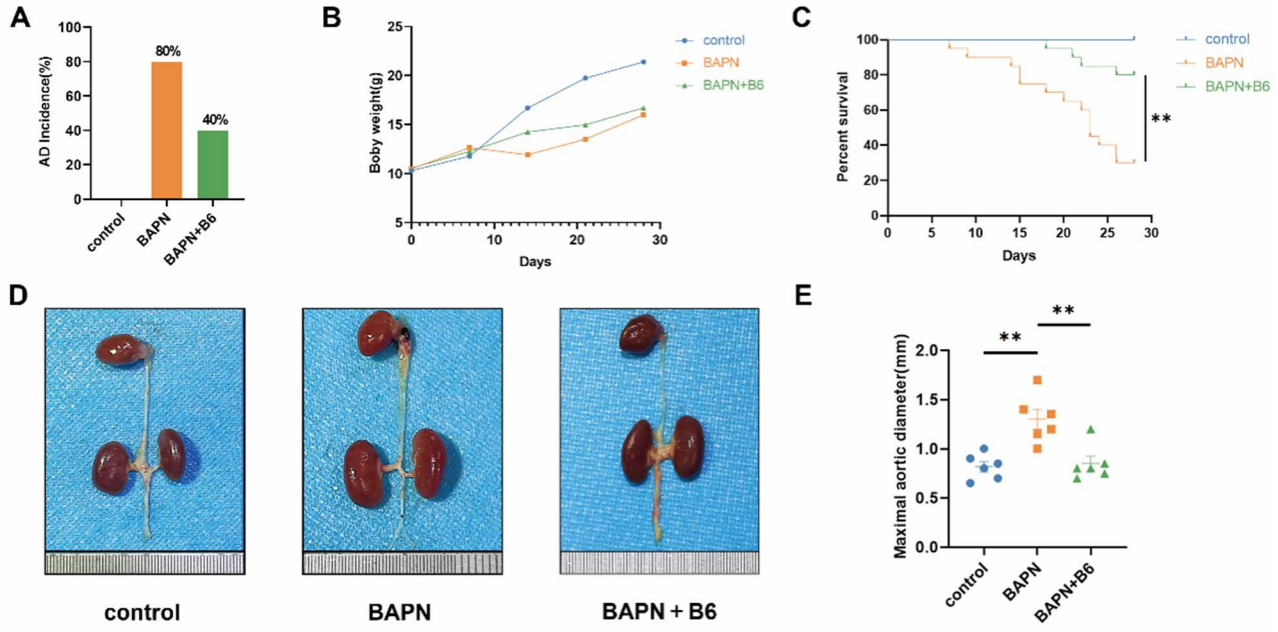

Fig. 1: B6 reduces the incidence of AD.
(A) AD incidence in C57BL-6 mice in each group; (B) Body weight changes during model induction; (C) Survival curve of C57BL-6 mice in each group (n=20); (D) Macroscopic images of the aorta in each group; (E) Maximal thoracic aortic diameter in each group. (n=6). *p<0.05, **p<0.01, ***p<0.001.

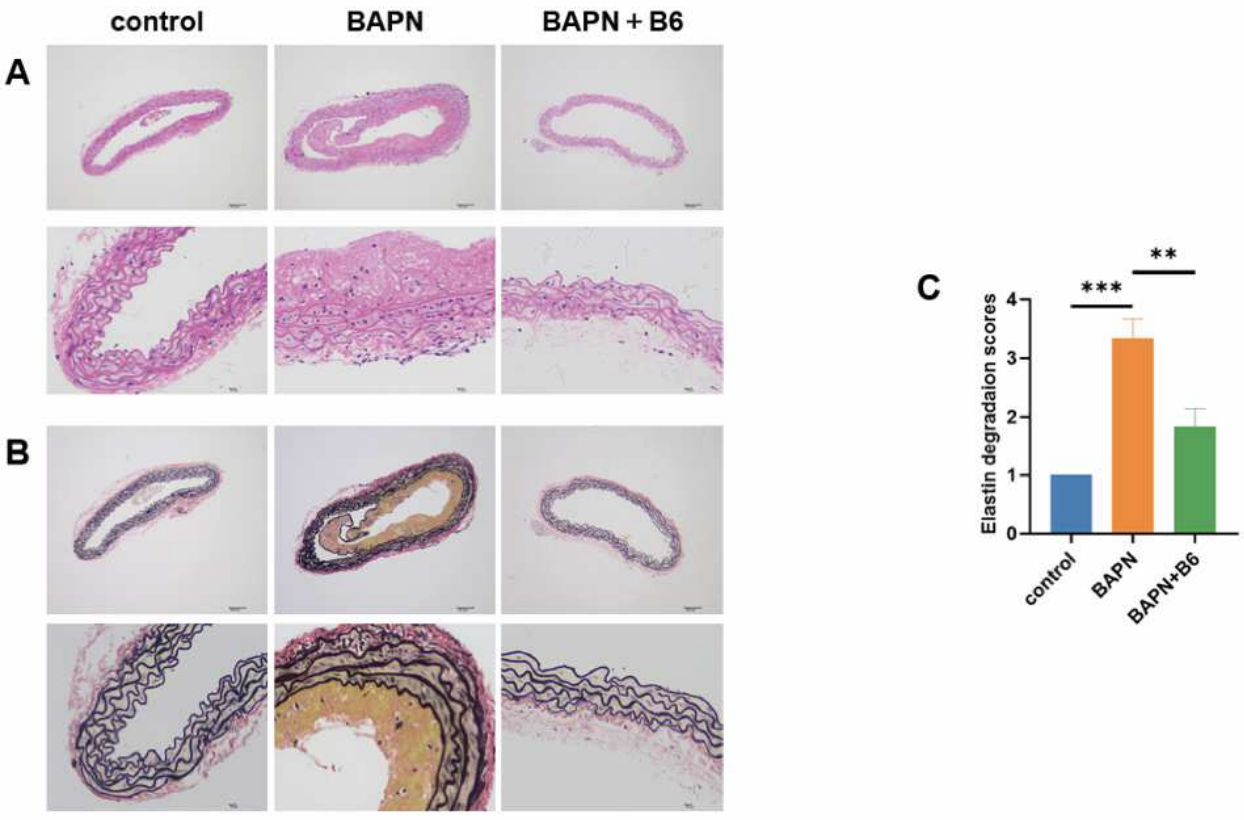

Fig. 2: Microscopic images of (A) HE and (B) EVG staining of aortic sections in each group. The scale bar of each image :100μm;10μm; (C) Statistical analysis of elastin fragmentation (n=6). Data are expressed as mean ± SD. Statistical significance: *p<0.05, **p<0.01, ***p<0.001.

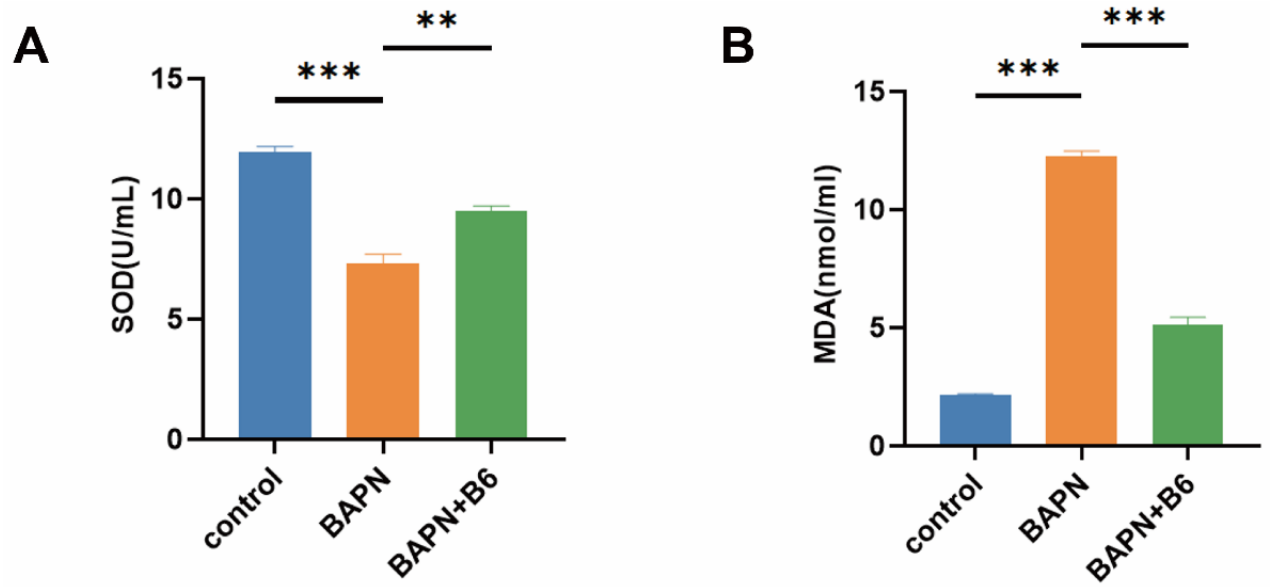

Fig. 3: (A) MDA and (B) SOD levels. *p<0.05, **p<0.01, ***p<0.001.

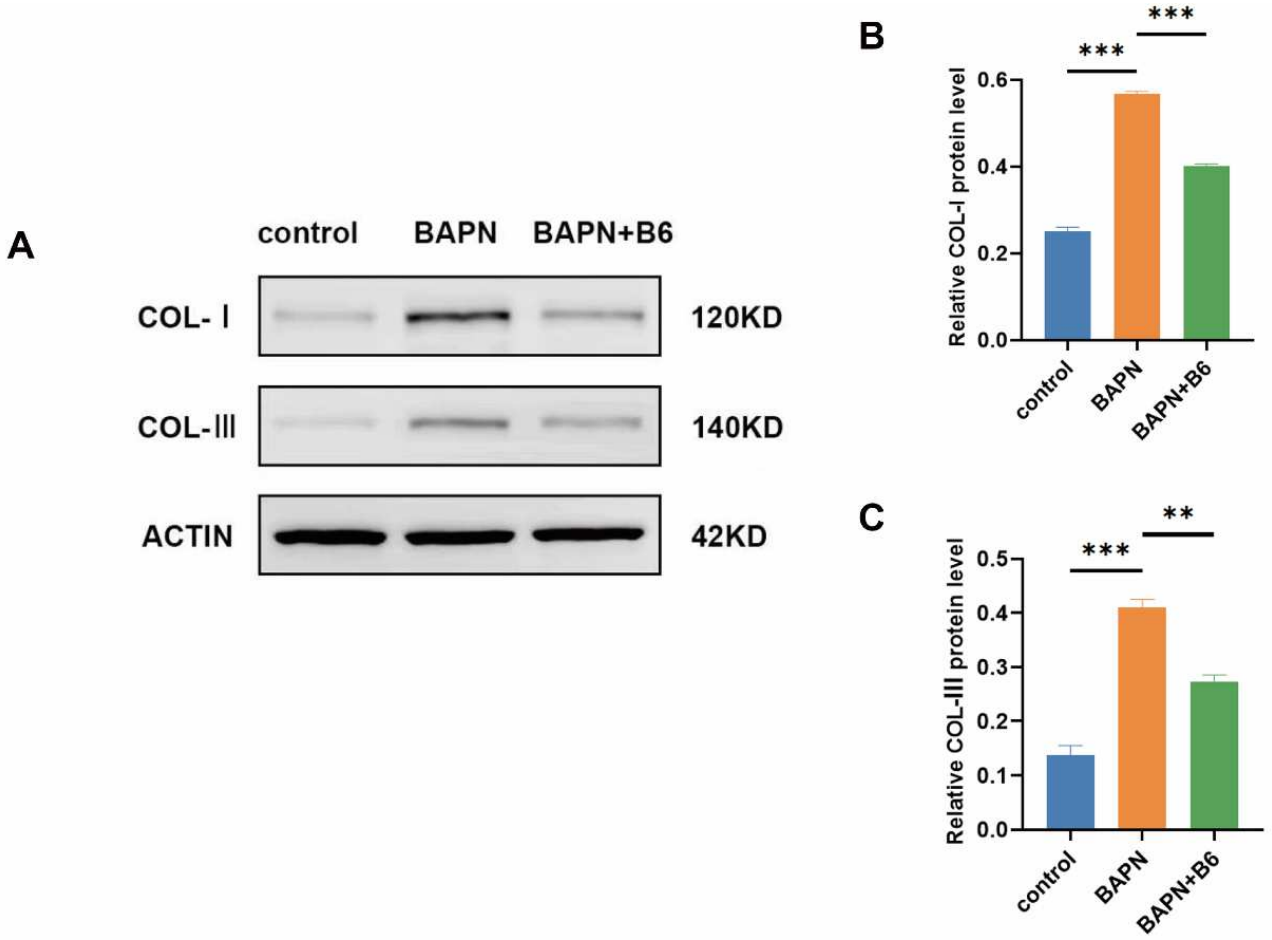

Fig. 4: (A) Western blot of COL-I and COL-III proteins in each group; (B) Relative COL-I protein level; (C) Relative COL-III protein level. *p<0.05, **p<0.01, ***p<0.001.

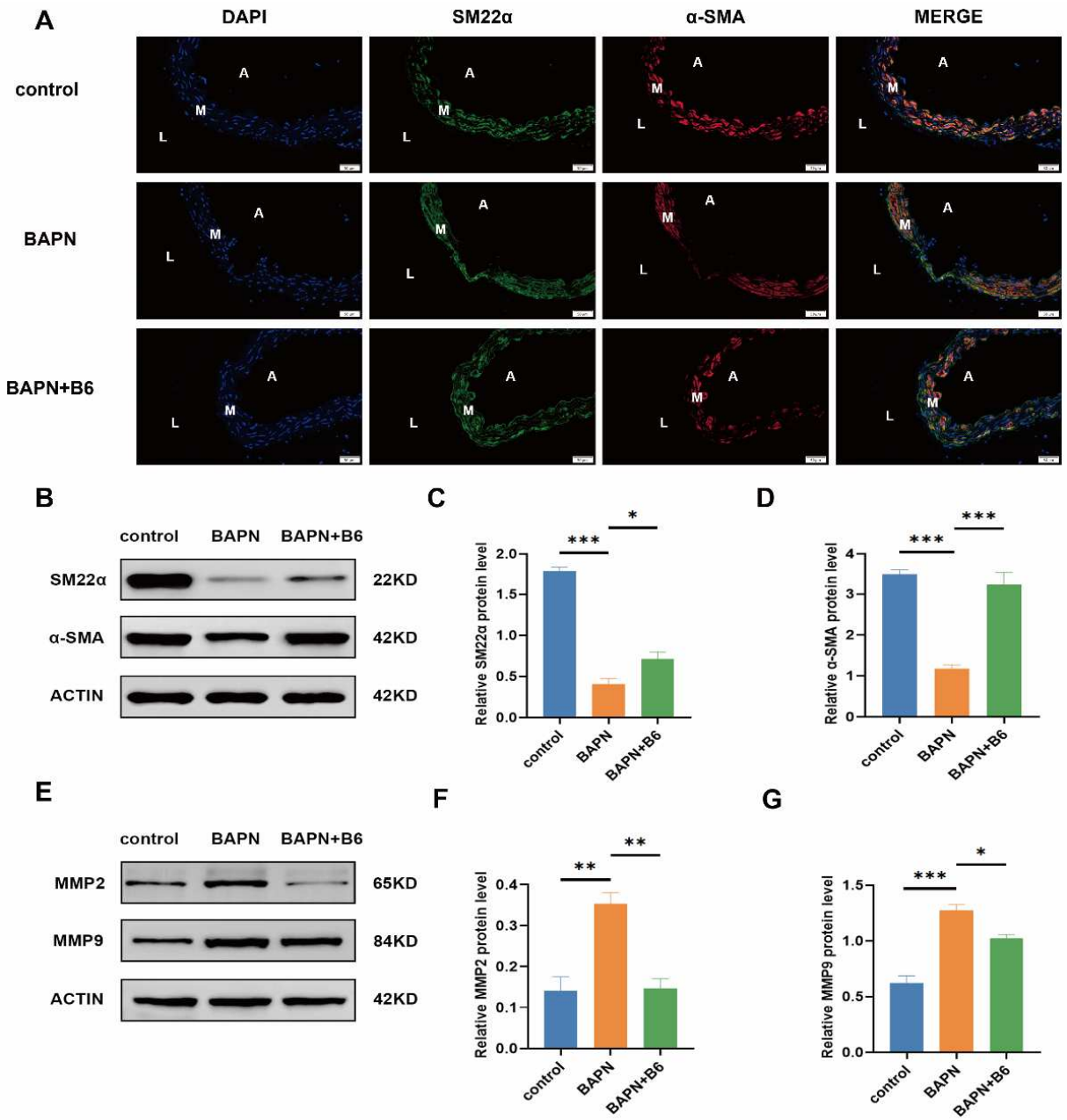

Fig. 5: B6 regulates contractile protein degradation and mitigates cell death during aortic dissection. (A) Representative images of α-SMA and SM22α immunofluorescence staining of the aortas. DAPI (blue). SM22α (Green). SMA (Red). Scale bars: 50μm. (n=6 per group). A, adventitia; M, medium; L, lumen; (B) Western blot images of SM22α and α-SMA in each group; (C-D) Statistical analysis of SM22α and α-SMA protein levels; (E) Western blot images of MMP2 and MMP9 in each group; (F-G) Statistical analysis of MMP2 and MMP9 protein levels. *p<0.05, **p<0.01, ***p<0.001.

Elevated MDA levels and reduced SOD expression have been observed in thoracic aortic tissues of patients with AD. This study revealed significant elevations in plasma MDA levels and diminished SOD activity in the BAPN group, while B6 treatment resulted in decreased MDA levels and enhanced SOD activity in the BAPN-induced mice. Considering these findings, impaired antioxidant systems and increased oxidative stress in the aortic wall are likely contributors to the development of AD. Thus, B6 may act as a protective and preventive agent against AD by mitigating oxidative stress.

ECM constitutes the primary component of the medial layer of the aortic vessels (Wu *et al*., 2013). ECM degradation substantially impairs the stability of aortic structures. Matrix Metalloproteinases (MMPs), specialized proteolytic enzymes, are synthesized by immune cells in reaction to inflammatory stimuli and are crucial for the destruction of elastic fibers and collagen (Koullias, Ravichandran, Korkolis, Rimm, and Elefteriades, 2004; Zhang *et al*., 2014). Studies have shown that in SOCS3-deficient mice, there is a marked decrease in SOCS3 expression and an elevation in STAT signaling protein

levels in the aortic tissues (Murphy, King, and Leckie, 2020). This results in an influx of inflammatory cells and a significant increase in MMP-2 and MMP-9 expression, which accelerate ECM degradation. This study is the first to reveal the protective effects of B6 against ECM degradation, thereby potentially mitigating AD progression. Under pathological conditions, VSMCs undergo dedifferentiation and adopt a synthetic phenotype (Rombouts *et al*., 2022). These synthetic VSMCs promote ECM degradation by secreting elevated levels of MMPs, which impair the vascular wall. Oxidative stress is a critical factor in initiating the VSMC transformation. Chronic hypoxia causes homeostatic imbalance and vascular remodeling, predisposing patients to aortic dissection (Faraci and Didion, 2004). Liu *et al*.' research showed that Alpha-lipoic acid inhibited aortic dissection by several inhibiting the oxidative stress and the VSMC phenotype transformation, further decreasing the expression of MMP-2 and MMP-9, which may reduce the elastin degradation (Liu, *et al.*, 2022). Similarly, our study indicated that vitamin B6 could inhibit VSMC conversion, potentially hindering the progression of aortic dissection.

CONCLUSION

This study is the first to explore B6's protective role in aortic injury, as demonstrated by its ability to mitigate ECM degradation and inhibit VSMC transformation. However, the exact mechanisms behind these outcomes remain inadequately comprehended and necessitate additional inquiry. Nonetheless, these results indicate a substantial role of B6 in ameliorating AD.

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Author's contributions
All authors contributed to the study conception and reviewed the manuscript. Ru Chen: Writing-original draft, validation, investigation, methodology, conceptualization; Dongkai Gao: Writing-original draft, validation, investigation, methodology; Wuyi Ban: Writing-review and editing, methodology, formal analysis; Liying Qiu: Writing-review and editing, methodology, formal analysis; Zangjia Geng: Resources; Lei Song: Conceptualization, validation, resources, project administration, writing-review and editing.

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Data availability statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval
The study was conducted in accordance with the Guide for the Care and Use of Laboratory Animals of the National Research Council (NRC). Ethical approval was obtained from the Institutional Animal Care and Use Committee of Southwest Minzu University, Chengdu, China (Approval No. 2023MDLS059).

Conflict of interest
The authors declare no competing interests.

REFERENCES

Chakraborty R, Saddouk FZ, Carrao AC, Krause DS, Greif DM and Martin KA (2019). Promoters to study vascular smooth muscle. *Arterioscler Thromb Vasc Biol.,* **39**(4): 603-612.

Di Salvo ML, Contestabile R and Safo MK (2011). Vitamin B(6) salvage enzymes: Mechanism, structure and regulation. *Biochim Biophys Acta,* **1814**(11): 1597-1608.

Emeto TI, Moxon JV, Au M and Golledge J (2016). Oxidative stress and abdominal aortic aneurysm: Potential treatment targets. *Clin. Sci. (Lond),* **130**(5): 301-315.

Faraci FM and Didion SP (2004). Vascular protection: Superoxide dismutase isoforms in the vessel wall. *Arterioscler Thromb Vasc Biol,* **24**(8): 1367-1373.

Friso S, Lotto V, Corrocher R and Choi SW (2012). Vitamin B6 and cardiovascular disease. *Subcell Biochem,* **56**: 265-290.

Kazaleh M and Gioscia-Ryan R (2023). Oxidative stress and the Pathogenesis of Aortic Aneurysms. *Biomedicines,* **12**(1): 3.

Liu R, Huang SS, Shi H, Chang S and Ge J (2022). Alpha-lipoic acid protects against aortic aneurysm and dissection by improving vascular smooth muscle cell function. *Life Sci,* **311**(Pt A): 121159.

Mascolo E and Vernì F (2020). Vitamin B6 and diabetes: Relationship and molecular mechanisms. *Int. J. Mol. Sci.,* **21**(10): 3669.

Murphy MP, King JR and Leckie KE (2020). Deletion of socs3 expression in aortic smooth muscle cells ameliorates aortic dissection. *JACC Basic Transl Sci.,* **5**(2): 145-147.

Nakashima Y, Shiokawa Y and Sueishi K (1990). Alterations of elastic architecture in human aortic dissecting aneurysm. *Lab Invest,* **62**(6): 751-760.

Nienaber CA, Clough RE, Sakalihasan N, Suzuki T, Gibbs R, Mussa F and Pepper J (2016). Aortic dissection. *Nat Rev Dis Primers,* **2**: 16053.

Prasad K, McNair ED, Qureshi AM and Casper-Bell G (2012). Vitamin E slows the progression of hypercholesterolemia-induced oxidative stress in heart, liver and kidney. *Mol. Cell Biochem,* **368**(1-2): 181-187.

Pape LA, Awais M, Woznicki EM, Suzuki T, Trimarchi S, Evangelista A and O'Gara P (2015). Presentation, diagnosis, and outcomes of acute aortic dissection: 17-

Year trends from the international registry of acute aortic dissection. *J Am Coll Cardiol,* **66**(4): 350-358.

Rombouts KB, van Merrienboer TAR, Ket JCF, Bogunovic N, van der Velden J and Yeung KK (2022). The role of vascular smooth muscle cells in the development of aortic aneurysms and dissections. *Eur. J. Clin. Invest,* **52**(4): e13697.

Ren C, Wu W, Chen R, Gu J, Wu L and Song L (2025). Allicin alleviates aortic dissection progression via p38/MAPK/NF-κB signaling pathways. Jundishapur *J. Nat. Pharm. Prod.*, **20**(4): e165405.

Ren WH, Liu Y, Wang XR, Jia LX, Piao CM, Lan F and Du J (2016). β-Aminopropionitrile monofumarate induces thoracic aortic dissection in C57BL/6 mice. *Sci Rep.,* **6**: 28149.

Strobel NA, Fassett RG, Marsh SA and Coombes JS (2011). Oxidative stress biomarkers as predictors of cardiovascular disease. *Int. J. Cardiol.,* **147**(2): 191-201.

Shen YH, LeMaire SA, Webb NR, Cassis LA, Daugherty A and Lu HS (2020). Aortic aneurysms and dissections series: Part II: Dynamic signaling responses in aortic aneurysms and dissections. *Arterioscler Thromb Vasc Biol,* **40**(4): e78-e86.

Watanabe M and Sawai T (1999). Alteration of cross-linking amino acids of elastin in human aorta in association with dissecting aneurysm: Analysis using high performance liquid chromatography. *Tohoku J. Exp. Med.,* **187**(4): 291-303.

Wu D, Shen YH, Russell L, Coselli JS and LeMaire SA (2013). Molecular mechanisms of thoracic aortic dissection. *J. Surg. Res.,* **184**(2): 907-924.

Yang C, Meng X, Xia C, Sun Y, Ren Y, Wang J, Li Y and Wang X (2025). IGFBP2 plays a key role in aerobic exercise-mediated inhibition of ferroptosis in cardiac ischemia/reperfusion (I/R) injury. *J. Transl Med,* **23**: 1080.

Zhang YF, Li M, Cui E, Zhang H, Zhu X, Zhou J, Yan M and Sun J (2020). Dexmedetomidine attenuates sevoflurane-induced neurocognitive impairment through α2-adrenoceptors. *Molecular Medicine Reports,* **22**(5): 3927-3939.

Zhou Y, Wang T, Fan H, Liu S, Teng X, Shao L and Shen Z (2024). Research progress on the pathogenesis of aortic aneurysm and dissection in metabolism. *Curr Probl Cardiol.,* **49**(1 Pt A): 102040.

Zhou Z, Cecchi AC, Prakash SK and Milewicz DM (2022). Risk factors for thoracic aortic dissection. *Genes (Basel),* **13**(10): 1814.

Zhu Y, Lingala B, Baiocchi M, Tao JJ, Toro Arana V, Khoo JW and Woo YJ (2020). Type a aortic dissection-experience over 5 decades: JACC Historical breakthroughs in perspective. *J Am Coll Cardiol,* **76**(14): 1703-1713.