Article

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Pachymic Acid A Alleviates Myocardial Injury in Acute Myocardial Infarction Mice by Regulating the AMPK/mTOR Pathway-Mediated Autophagy

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Background: Despite significant advances in therapeutic approaches, the overall prognosis of acute myocardial infarction (AMI) patients remains poor. *Poria cocos*, a traditional edible medicinal fungus, contains Pachymic acid A (PAA), a triterpenoid compound recognized for its potent anti-inflammatory properties across various inflammatory conditions. Therefore, we investigated the effects of PAA in a murine AMI model and explored its underlying mechanisms.

Methods: AMI was induced in mice by tying the left anterior descending (LAD) coronary artery, and the model mice were treated with different concentrations of PAA. Histological staining was employed to assess cardiac tissue injury. Oxidative stress markers and inflammatory cytokines in myocardial tissues were quantified using Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR). and biochemical assays. Apoptotic cardiomyocytes were identified via the Terminal deoxynucleotidyl transferase dUTP Nick End Labeling (TUNEL) assay. Immunoblotting was conducted to quantify autophagy-associated proteins (Microtubule-associated protein 1A/1B light chain 3 (LC3) II/LC3I, Beclin1, p62) and the AMP-activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) signaling pathway.

Results: PAA treatment significantly reduced myocardial injury and fibrosis in AMI mice. It suppressed the expression levels of pro-inflammatory cytokines Tumor Necrosis Factor (TNF)-α, Interleukin (IL)-6, and IL-1β, decreased malondialdehyde (MDA), and icreased glutathione peroxidase (GSH-Px) activity ($p < 0.05$). Furthermore, PAA attenuated cardiomyocyte apoptosis and enhanced autophagy, as evidenced by elevated LC3II/LC3I and Beclin1 expression and reduced p62 levels. The AMPK pathway was found to be activated due to increased p-AMPK/AMPK ratios and reduced p-mTOR/mTOR expression ($p < 0.05$).

Conclusion: PAA may reduce AMI-induced cardiac injury by activating AMPK signaling and promoting autophagy, thereby reducing inflammation, oxidative stress, and apoptosis in myocardial tissue.

Keywords: Pachymic acid A; acute myocardial infarction; inflammation; oxidative stress; autophagy; apoptosis; AMPK

Introduction

Acute myocardial infarction (AMI) remains a leading cause of morbidity and mortality worldwide [1]. Although significant therapeutic advances, such as percutaneous coronary interventions, surgical techniques, and adjunctive pharmacological therapies, have improved symptom management, long-term outcomes for AMI patients remain suboptimal [2]. The loss of cardiomyocytes, whether due to acute or chronic injury, increases oxidative stress and induces inflammatory responses, ultimately resulting in impaired cardiac function and a higher risk of heart failure [3]. Therefore, identifying effective therapeutic agents, particularly those derived from natural sources, continues to be a crucial area in AMI management.

Autophagy plays a critical role in maintaining cellular homeostasis by facilitating the degradation and recycling of damaged organelles, misfolded proteins, and other cytoplasmic components [4] via the autophagosome–lysosome fusion pathway. This process supports cell integrity, particularly under stress conditions. Dysregulated autophagy has been associated with the development and progression of AMI, and growing evidence suggests that enhancing autophagic activity may confer cardioprotective benefits [5].

Natural products are gaining increasing attention as potential therapeutic agents for managing cardiac diseases. *Poria cocos*, a traditional medicinal and edible fungus, contains Pachymic acid A (PAA), a bioactive tetracyclic triterpenoid found as its primary active constituent. Previous research has shown that PAA attenuates renal fibrosis and preserves renal function by upregulating Sirt3 expression [6]. In diabetic nephropathy models, PAA has been demonstrated to induce mitochondrial autophagy, as evidenced by elevated expression of Microtubule-associated protein 1A/1B light chain 3 (LC3) and Autophagy-related protein 5 (ATG5). and reduced levels of p62 and FUNDC1 in podocytes and renal tissues exposed to high glucose conditions [7]. Furthermore, PAA has been found to enhance

angiogenesis and promote the migratory capability of human cardiac microvascular endothelial cells under oxygen-glucose deprivation [8].

However, the specific effects and underlying mechanisms of PAA in AMI, especially its role in modulating inflammation, oxidative stress, and autophagy, remain unclear. We investigated the therapeutic potential of PAA in a mouse model of AMI, focusing on its impact on myocardial inflammation, oxidative stress, and autophagic activity, potentially mediated via the AMP-activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) signalling pathway.

Materials and Methods

Experimental Animals and Establishment of the AMI Model

A total of 52 male and female C57BL/6 mice (8 weeks old, weighing 20–25 g) were obtained from the Jilin Provincial Medical Experimental Animal Center. Mice were housed under standard laboratory conditions (temperature: 22 ± 2 °C; humidity: 40–60%; 12-hour light/dark cycle), with ad libitum food and water.

Myocardial infarction was induced by ligating the left anterior descending (LAD) coronary artery under deep anesthesia using an intraperitoneal injection of pentobarbital sodium (60 mg/kg) [9]. Successful induction of infarction was confirmed by the development of pallor and cyanosis in the left ventricle and apex. The success rate of AMI model development was 92.3%, with 36 out of 39 mice demonstrating confirmed AMI. After 30 minutes, the ligature and silicone tubing were removed to initiate reperfusion, which was maintained for 120 minutes. Mice in the sham group underwent similar surgical interventions, except for LAD ligation.

The animals were randomly divided into five groups, with 6 mice per group): (1) Sham-operated control; (2) AMI model; (3) AMI + PAA (10 mg/kg); (4) AMI + PAA (20 mg/kg); (5) AMI + PAA (20 mg/kg) + Compound C (0.2 mg/kg). PAA (Sigma-Aldrich, P00123, St. Louis, Missouri, USA) was administered once daily via oral gavage (10/20 mg/kg), starting immediately after surgery and continued for four consecutive weeks. In the AMI + PAA + Compound C group, mice received an intraperitoneal injection of Compound C (0.2 mg/kg), an AMPK inhibitor, 30 minutes before each PAA administration to inhibit AMPK signaling [10].

Mice were monitored every hour for the initial 12 hours following surgery to assess clinical signs and postoperative recovery. After the end of the treatment phase, mice were euthanized via an intraperitoneal injection of sodium phenobarbital (150 mg/kg). Blood samples (500 µL) and cardiac tissues were then harvested for subsequent analyses.

All experimental procedures were performed following institutional guidelines and approved by the Animal Ethics Committee of the Affiliated Hospital of Changchun University of Chinese Medicine, China (Approval Number: 2024746).

Tissue Staining

Cardiac tissues were fixed in 4% paraformaldehyde for 24 hours, followed by dehydration and paraffin-embedding. Paraffin blocks were cut into 4 µm-thick sections and stained with hematoxylin-eosin (H&E, Sigma-Aldrich, HHS32, St. Louis, MO, USA) and Masson's trichrome (Sigma-Aldrich, 120440, St. Louis, MO, USA) to assess cardiac morphology and fibrosis.

For H&E staining, tissue sections were treated with hematoxylin for 5–10 minutes, then differentiated in 1% hydrochloric acid ethanol for 10–30 seconds, and counterstained with alkaline eosin for 1–2 minutes. After that, tissue sections were dehydrated through graded ethanols, cleared in xylene, and examined under a light microscope.

Furthermore, Masson's trichrome staining was conducted by sequential incubation with Weigert's iron hematoxylin for 10 minutes, Biebrich scarlet-acid fuchsin for 10 minutes, and phosphomolybdic acid, with phenol fuchsin for 5 minutes. After a thorough wash, tissue sections were dehydrated, cleared with xylene, and mounted for histological examination under light microscopy.

Detection of Cardiac Troponin I, MDA, and GSH-Px

Cardiac troponin I (cTnI) levels in myocardial tissue were quantified using a commercial Enzyme-Linked Immunosorbent Assay (ELISA) kit (ab108812, Abcam, Cambridge, UK) following the manufacturer's instructions. Approximately 20 mg of Myocardial tissue was homogenized in PBS, and the resulting supernatant was collected. Total protein content was quantified using a Bicinchoninic Acid Assay (BCA) assay kit (23225, Thermo Fisher Scientific, Waltham, MA, USA). Furthermore, malondialdehyde (MDA) and glutathione geroxidase (GSH-Px) levels were evaluated using colorimetric assay kits (MAK085 and CS0260, Sigma-Aldrich, St. Louis, MO, USA).

Terminal Deoxynucleotidyl Transferase dUTP Nick End Labeling (TUNEL) Staining

Paraffin-embedded cardiac tissue sections (4 µm) were stained using a TUNEL apoptosis detection kit (11684795910, Roche, Basel, Switzerland), followed by nuclear counterstaining with DAPI (Thermo Fisher Scientific, D1306, Waltham, MA, USA). The stained tissue sections were evaluated using confocal fluorescence microscopy to determine the rate of apoptosis.

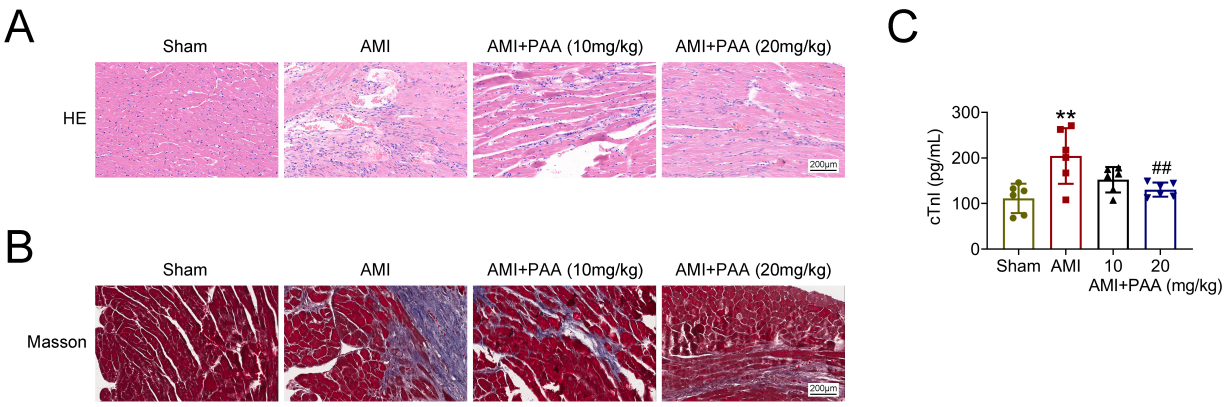

Fig. 1. PAA attenuates myocardial injury in the AMI mice. (A) H&E staining assessed myocardial pathology. (B) Masson's trichrome staining evaluated fibrosis. (C) Serum cTnI levels were measured using ELISA. Data: mean ± SEM, n = 6; 4 weeks post-surgery; three sections/samples. $^{**}p < 0.01$ vs. Sham; $^{\#\#}p < 0.01$ vs. AMI. PAA, Pachymic acid A; AMI, acute myocardial infarction; H&E, hematoxylin-eosin; cTnI, Cardiac Troponin I; ELISA, Enzyme-Linked Immunosorbent Assay; SEM, standard error of the mean.

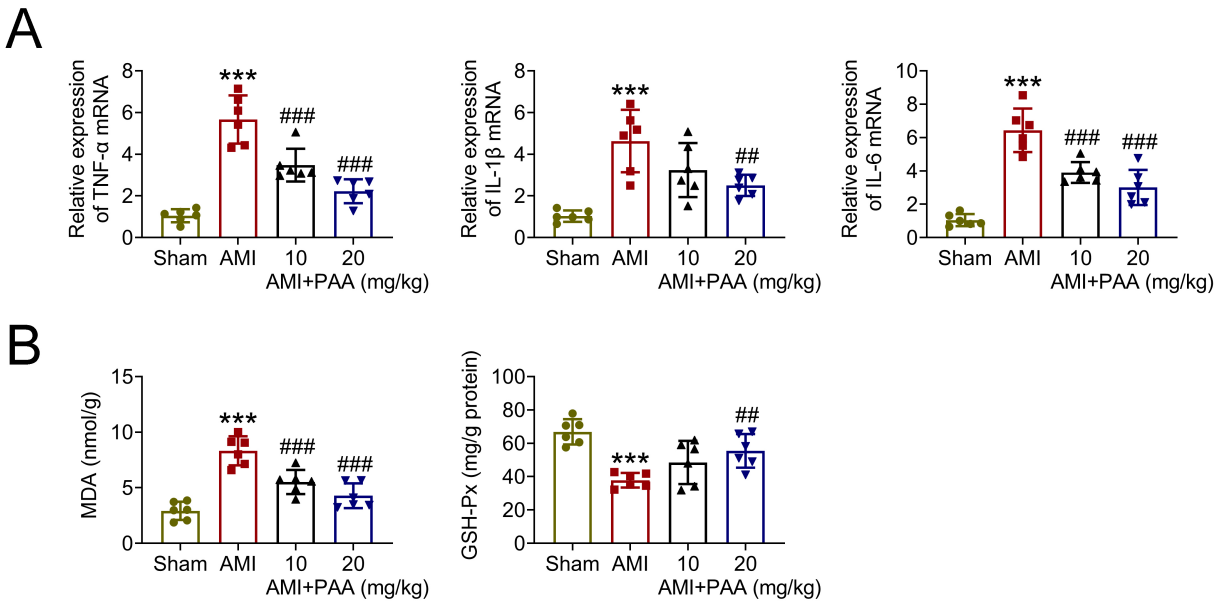

Fig. 2. PAA reduces myocardial inflammation and oxidative stress in the AMI mice. (A) qRT-PCR quantified myocardial TNF-α, IL-1β, and IL-6 mRNA levels. (B) MDA content and GSH-Px activity were determined using assay kits. Data: mean ± SEM, n = 6. $^{***}p < 0.001$ vs. Sham; $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ vs. AMI. qRT-PCR, quantitative Reverse Transcription Polymerase Chain Reaction; TNF, Tumor Necrosis Factor; IL, Interleukin; MDA, malondialdehyd; GSH-Px, glutathione peroxidase.

Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR)

Total RNA was isolated from mouse cardiac tissue using TRIzol reagent (15596026, Invitrogen, Carlsbad, CA, USA), following the manufacturer's instructions. Complementary DNA (cDNA) was synthesized using the PrimeScript RT reagent kit (RR037A, Takara Bio Inc., Shiga, Japan). The qRT-PCR was performed employing SYBR Green PCR Master Mix (Takara Bio Inc.,RR820A, Kusatsu, Shiga, Japan), and gene-specific primers under optimized cycling conditions. Relative gene expression was determined using the $2^{-\Delta\Delta CT}$ method, with Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH) serving as the reference gene. Primer sequences used in this study were as follows: Interleukin (IL)-6: F: 5′-CTTCCATCCAGTTGCCTTCT-

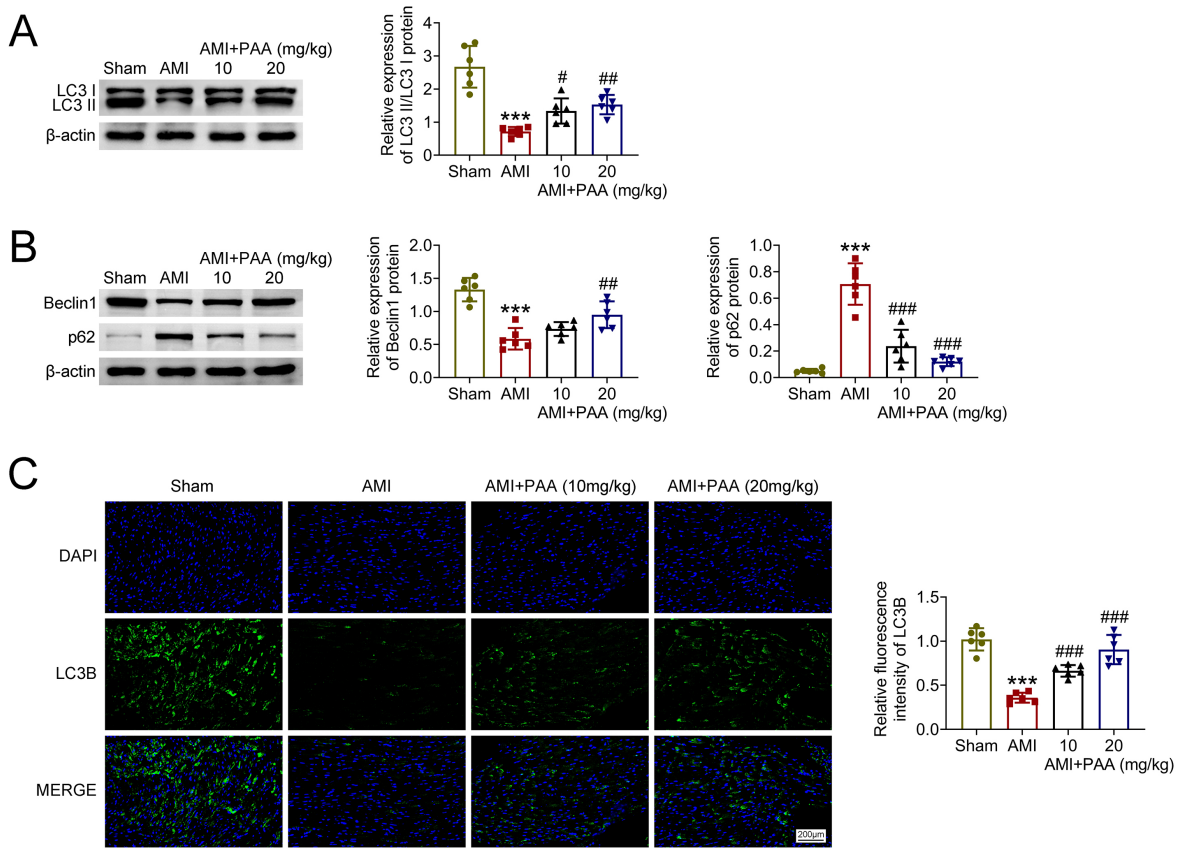

Fig. 3. PAA promotes autophagy in myocardial tissue of the AMI mice. (A) Western blot analysis of LC3II/LC3I. (B) Beclin1 and p62 protein levels. (C) LC3B expression assessed by immunofluorescence. Data: mean ± SEM, n = 6. ***$p < 0.001$ vs. Sham; $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ vs. AMI. LC3, Microtubule-associated protein 1A/1B light chain 3.

3′; R: 5′-CCTTCTGTGACTCCAGCTTATC-3′ IL-1β: F: 5′-CTTCCAGGATGAGGACATGAG-3′; R: 5′-TCACACACCAGCAGGTTATCG-3′ Tumor Necrosis Factor (TNF)-α: F: 5′-CCCTCACACTCAGATCATCTTCT-3′; R: 5′-GCTACGACGTGGGGCTACAG-3′ GAPDH: F: 5′-TGCACCACCAACTGCTTAGC-3′; R: 5′-GGCATGGACTGTGGTCATGAG-3′.

Immunofluorescence

Cardiac tissues were fixed, embedded in paraffin, and sectioned (4 μm) for immunofluorescence analysis, Tissue sections were stained with primary antibodies against LC3B (1:500, #AF4650, Affinity Biosciences, Cincinnati, OH, USA) and p-AMPK (1:500, #AF3423, Affinity Biosciences, Cincinnati, OH, USA), followed by incubation with HRP-conjugated secondary antibodies, anti-mouse IgG (1:1000, #S0002, Affinity Biosciences, Cincinnati, OH, USA) and anti-rabbit IgG (1:1000, #S0001, Affinity Biosciences, Cincinnati, OH, USA). The nuclei were counterstained with DAPI, and the stained tissue sections were examined under confocal fluorescence microscopy. The fluorescence intensity was quantitatively analyzed using image software (Image J version 8.0, National Institutes of Health, Bethesda, Maryland, USA).

Western Blotting

Myocardial tissue was ground into powder under liquid nitrogen and then lysed using RIPA buffer (R0278, Sigma-Aldrich, St. Louis, MO, USA) to extract total protein. Protein levels were assessed by BCA assay. Proteins were then resolved by SDS-PAGE and were subsequently transferred to PVDF membranes. Membranes then underwent overnight incubations with specific primary antibodies against LC3I (1:1000, #AF4007), LC3II (1:1000, #AF4650), Beclin1 (1:1000, #AF5128), p62 (1:1000, #AF5384), B-cell lymphoma (Bcl)-2 (1:1000, #AF6139), Bcl-2 Associated X protein (Bax) (1:1000, #AF0120), p-AMPK (1:1000, #AF3423), AMPK (1:1000, #AF6423), p-mTOR (1:1000, #AF3308), mTOR (1:1000, #AF6308), and β-actin (1:3000, #AF7018). All these primary antibodies were purchased from Affinity (Jiangsu, China). The next day, membranes were washed and incubated with HRP-conjugated secondary antibodies, anti-mouse IgG (1:5000,

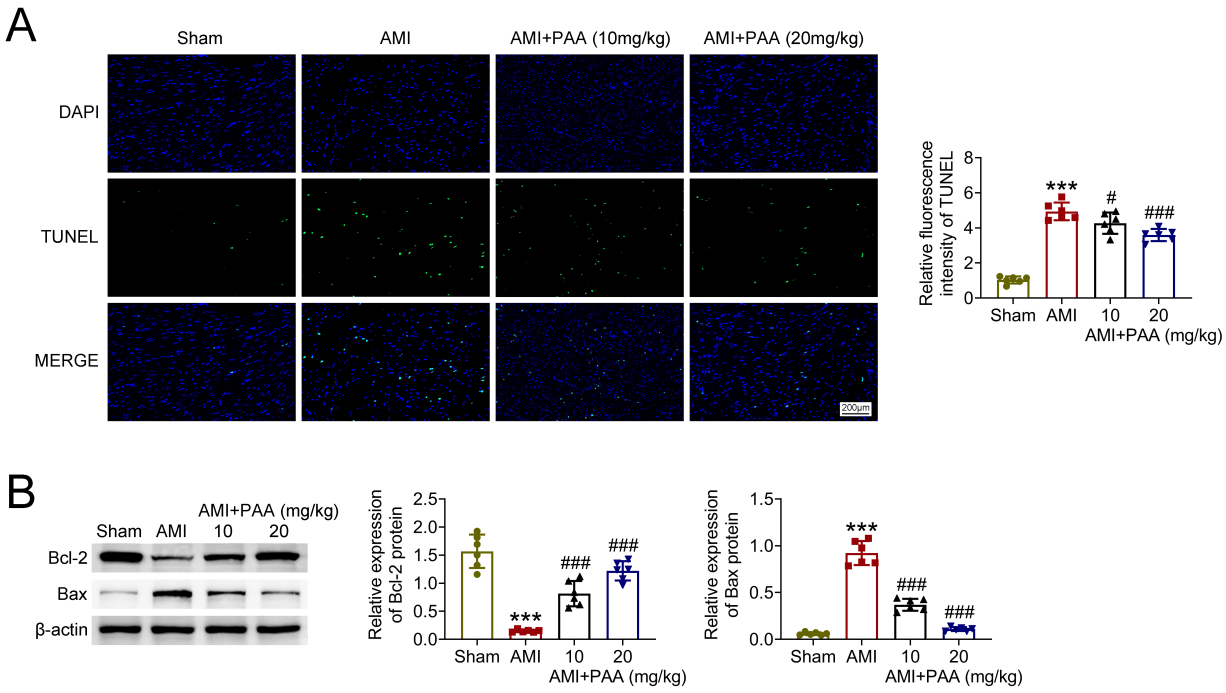

Fig. 4. PAA inhibits cardiomyocyte apoptosis in AMI mice. (A) TUNEL assay identified myocardial apoptosis. (B) Bcl-2 and Bax protein levels were examined using immunoblotting. Data: mean ± SEM, n = 6; 4 weeks post-operation; three sections per sample. ***$p < 0.001$ vs. Sham; $^{\#}p < 0.05$, $^{\#\#\#}p < 0.001$ vs. AMI. Bcl, B-cell lymphoma; Bax, Bcl-2 Associated X protein.

#S0002) and anti-rabbit IgG (1:5000, #S0001). Protein bands were visualized using an enhanced chemiluminescence (ECL) system, and band intensities were quantified through imaging analysis software.

Statistical Analysis

Statistical analysis was conducted using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Data were presented as mean ± standard error of the mean (SEM). Group differences were evaluated using one-way ANOVA, followed by Tukey's post hoc test for multiple comparisons. The Shapiro–Wilk test was used to assess data normality, and Levene's test was applied to examine homogeneity of variances. A p-value less than 0.05 was considered statistically significant.

Results

PAA Reduces Cardiac Damage in AMI Mice

Histological analysis revealed a significantly disrupted cardiomyocyte architecture and extensive infiltration of inflammatory cells in the myocardial tissue of AMI mice. These pathological features were markedly improved following PAA treatment (Fig. 1A). Masson trichrome staining further confirmed significant fibrotic changes in the infarcted myocardium, which were reduced significantly after PAA administration (Fig. 1B). Furthermore, serum cTnI levels were substantially elevated in the AMI group, whereas treatment with PAA (20 mg/kg) resulted in a pronounced reduction in cTnI levels (Fig. 1C, $p < 0.05$).

PAA Reduces Myocardial Inflammation and Oxidative Stress

The mRNA expression levels of pro-inflammatory cytokines TNF-α, IL-1β, and IL-6 were significantly increased in AMI mice (Fig. 2A), along with higher MDA levels and reduced GSH-Px activity (Fig. 2B). These findings indicate enhanced oxidative stress and impaired antioxidant capacity in these mice. However, PAA treatment significantly reversed these changes, reflecting its anti-inflammatory and antioxidative effects ($p < 0.05$).

PAA Enhances Autophagic Activity in AMI Mice

Immunoblotting demonstrated reduced Beclin1 and LC3II/LC3I expression, along with elevated p62 levels in cardiac tissues of AMI mice (Fig. 3A,B). These alterations indicated impaired autophagic flux in AMI mice. In contrast, PAA treatment elevated Beclin1 expression and the LC3II/LC3I ratio, while reducing p62 expression ($p < 0.05$). Consistent with these observations, immunofluorescence staining showed an increase in LC3B expression in the myocardium of PAA-treated mice, mirroring the protein expression patterns observed in Western blot analy-

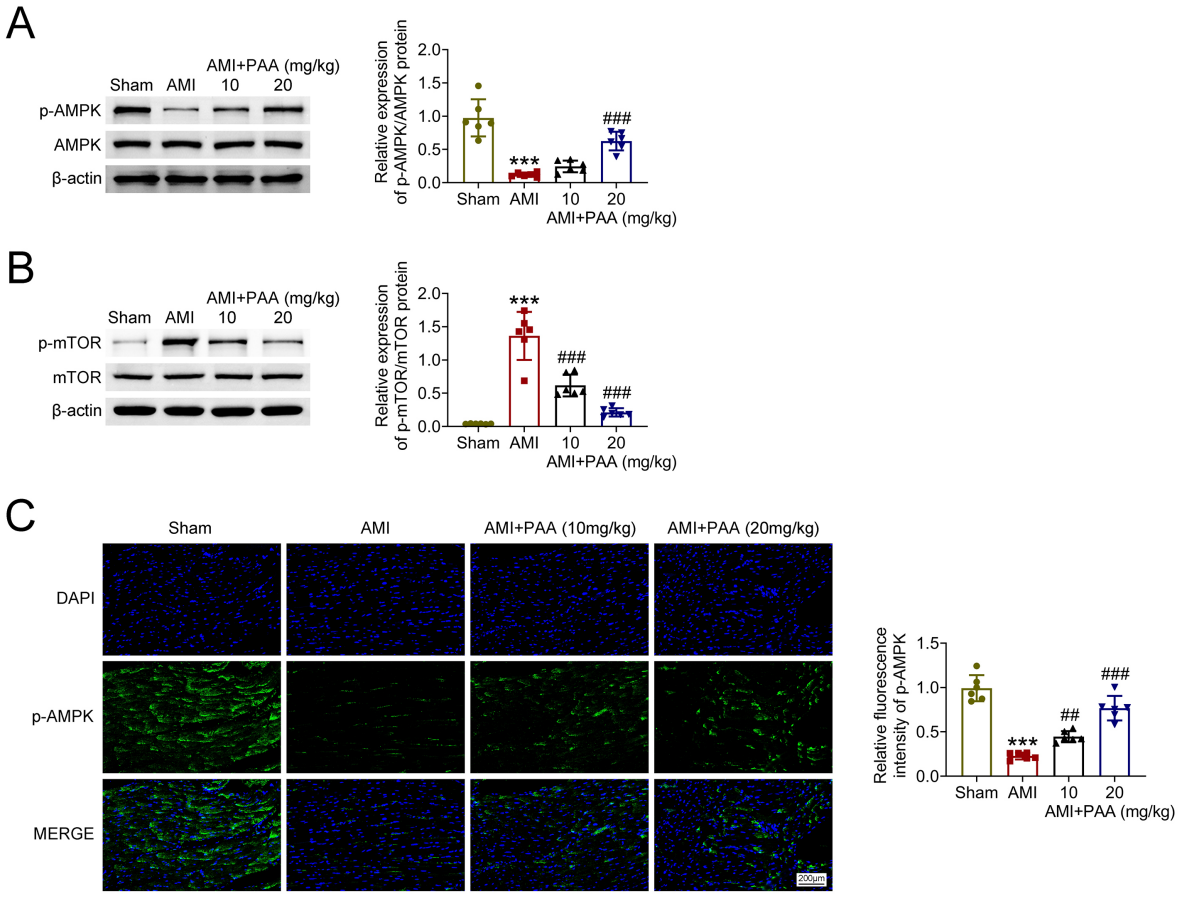

Fig. 5. PAA activates AMPK signaling in the myocardial tissue of the AMI mice. (A) Western blot analysis of phosphorylated and total AMPK (p-AMPK and AMPK) expression. (B) Western blot analysis of phosphorylated and total mTOR (p-mTOR and mTOR) expression. (C) Immunofluorescence staining of p-AMPK in myocardial tissue. Data are presented as mean ± SEM, n = 6. ***$p <$ 0.001 vs. Sham; $^{\#\#}p < 0.01$ vs. AMI; $^{\#\#\#}p < 0.001$ vs. AMI.

sis (Fig. 3C). Overall, these findings indicate that PAA enhances autophagic activity in the myocardium under AMI conditions.

PAA Suppresses Cardiomyocyte Apoptosis in AMI Mice

AMI mice showed a substantial increase in TUNEL-positive nuclei, reflecting elevated apoptotic activity (Fig. 4A, $p < 0.05$), along with increased Bax and decreased Bcl-2 levels (Fig. 4B, $p < 0.05$). However, PAA treatment significantly reduced the number of TUNEL-positive cells and Bax expression, while restoring Bcl-2 levels ($p < 0.05$), indicating that PAA effectively suppresses apoptosis in cardiac tissue under AMI conditions.

PAA Activates the AMPK Pathway in Myocardial Tissue

Given the crucial role of AMPK in modulating autophagy, immunoblotting revealed that AMI reduced the p-AMPK/AMPK ratio and increased the p-mTOR/mTOR ratio ($p < 0.05$). However, PAA treatment effectively reversed these effects by increasing p-AMPK/AMPK levels and decreasing p-mTOR/mTOR expression (Fig. 5A,B). Additionally, immunofluorescence staining further supports these findings, which confirmed elevated p-AMPK expression in the myocardium of PAA-treated mice (Fig. 5C, $p < 0.05$).

PAA Ameliorates Myocardial Injury via AMPK/mTOR-Mediated Autophagy

To further explore whether the cardioprotective effects of PAA are mediated via AMPK/mTOR-dependent autophagy, the AMPK inhibitor Compound C (0.2 mg/kg) was co-administered with PAA [11]. AMPK inhibition suppressed the autophagy-promoting effects of PAA and significantly reduced its protective impact on myocardial injury in AMI mice (Fig. 6, $p < 0.05$). These results suggest that the beneficial effects of PAA are mediated via the AMPK/mTOR signaling pathway.

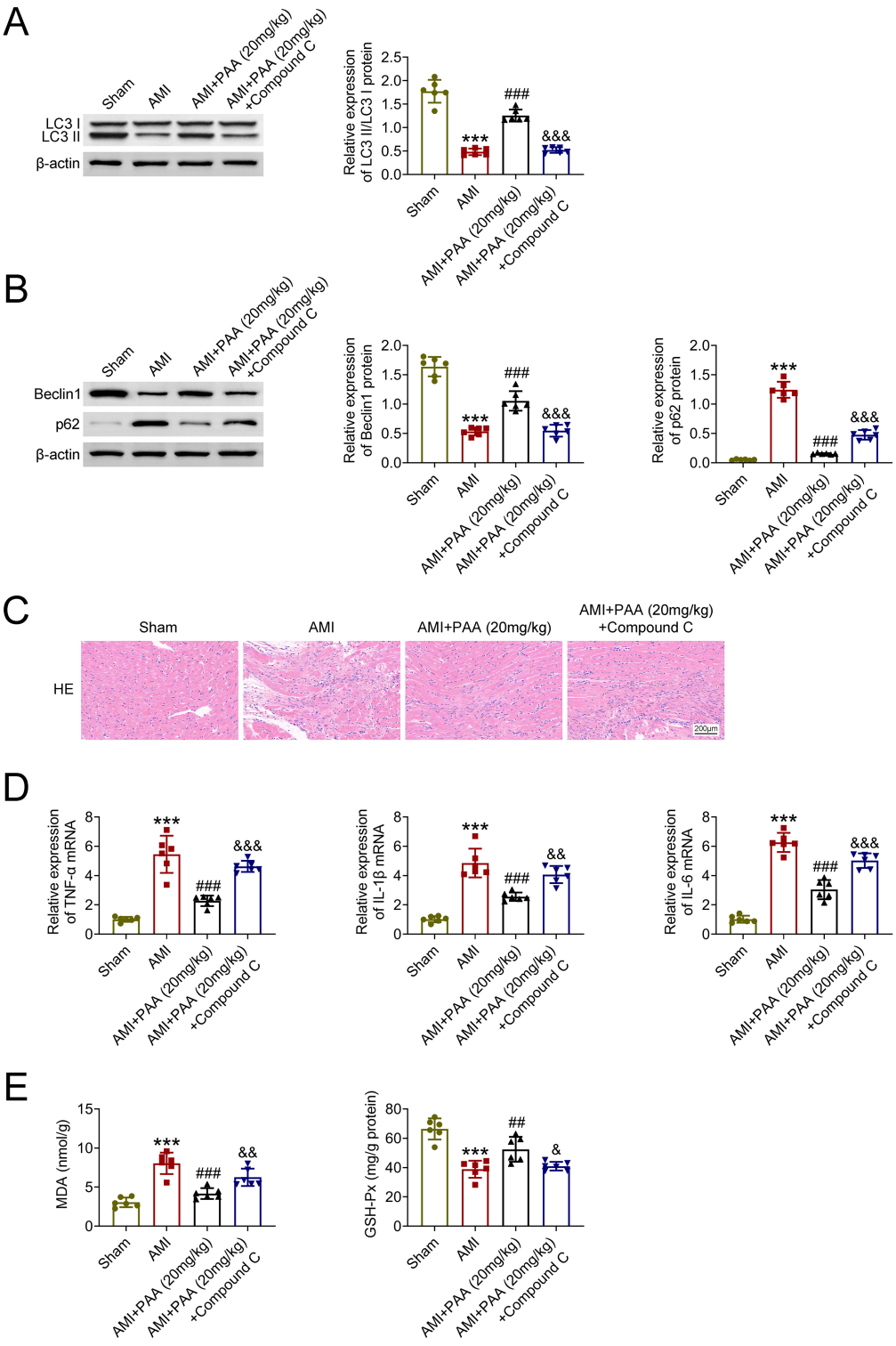

Fig. 6. PAA attenuates myocardial injury through AMPK/mTOR-mediated autophagy. (A) LC3II/LC3I, (B) Beclin1 and p62 protein levels were analyzed using Western blot analysis. (C) H&E staining evaluated myocardial histology. (D) TNF-α, IL-1β, and IL-6 mRNA levels were quantified using qRT-PCR. (E) MDA and GSH-Px levels were measured with assay kits. Data: mean $\pm$ SEM, n = 6; 4 weeks post-surgery; three sections/samples. ***$p < 0.001$ vs. Sham; $^{\#\#}p < 0.01$ vs. AMI, $^{\#\#\#}p < 0.001$ vs. AMI; $^{\&}p < 0.05$, $^{\&\&}p < 0.01$, $^{\&\&\&}p < 0.001$ vs. AMI + PAA (20 mg/kg).

Discussion

PAA, a triterpenoid monomer derived from *Poria cocos*, is recognized for its anti-inflammatory, antioxidant, anti-apoptotic and autophagy-promoting properties. Our previous *in vitro* study demonstrated that PAA attenuated oxygen–glucose deprivation-induced injury in human cardiac micro-vascular endothelial cells (HCMECs) by suppressing apoptosis, elevating the LC3-II/LC3-I ratio, and decreasing p62 expression, thereby activating autophagy via the AMPK/mTOR signaling pathway [8]. Building upon these in vitro findings, the present study employed a murine AMI model to investigate in vivo cardioprotective effects of PAA.

Oxidative stress and inflammation are pivotal drivers of cardiomyocyte death following AMI and contribute substantially to post-infarction heart failure. Reactive oxygen species (ROS) directly damage cellular constituents and increase the production of pro-inflammatory cytokines [12], which in turn recruit neutrophils, monocytes, and macrophages to the infarcted myocardium, further exacerbating myocardial injury [13]. In the current study, PAA treatment substantially downregulated myocardial expression of TNF-α, IL-6, and IL-1β, reduced lipid peroxidation (MDA), and restored GSH-Px activity. These findings underscore PAA's capacity to suppress both oxidative stress and inflammatory signalling in ischaemic cardiac tissue.

Autophagy plays a crucial role in modulating numerous physiological processes, such as inflammation and cardiovascular health. In cardiomyocytes, autophagy is particularly essential for maintaining mitochondrial integrity and supporting the high metabolic demands of the myocardium. As terminally differentiated cells, cardiomyocytes depend on efficient autophagic mechanisms to eliminate damaged mitochondria, misfolded proteins, and other dysfunctional organelles [14]. However, under certain pathological conditions, autophagy may contribute to cellular injury, and dysregulated autophagic activity has been implicated in various cardiovascular disorders. For instance, sodium-glucose co-transporter 2 (SGLT2) inhibitors have demonstrated cardioprotective effects, potentially through the suppression of excessive autophagy in myocardial tissue [15]. Conversely, increasing evidence suggests that autophagy serves as a protective and adaptive response to cellular stress in the myocardium, and its inhibition may accelerate the progression of heart failure. Previous research has revealed that Panax notoginseng saponins exert cardioprotective effects against AMI and heart failure by promoting autophagic activity [16]. In the present study, AMI resulted in the downregulation of Beclin1 and LC3II/LC3I expression and the upregulation of p62 protein in myocardial tissue, hallmarks of impaired autophagic flux. However, PAA treatment reversed these effects, increasing Beclin1 and LC3II/LC3I expression and reducing p62 levels, thereby indicating the reactivation of autophagy suppressed by AMI.

The AMPK–mTOR signaling pathway is a key upstream regulator of autophagy and plays a dual role in modulating cardiomyocyte apoptosis and maintaining myocardial energy homeostasis. AMPK is activated in response to increased AMP/ATP ratios during cellular energy stress and subsequently phosphorylates TSC2, resulting in the inhibition of mTOR and the activation of autophagy. Beyond its role in autophagic regulation, AMPK also inhibits apoptosis by increasing the Bcl-2/Bax ratio, thereby promoting cell survival under stress conditions [17]. In our study, myocardial tissue from AMI mice exhibited reduced AMPK phosphorylation and elevated mTOR expression, indicating disrupted energy signaling and suppressed autophagic activity. These abnormalities were significantly reversed following PAA treatment, suggesting that PAA exerts its cardioprotective effects, at least in part, by modulating the AMPK/mTOR signaling axis.

This study has several limitations that should be acknowledged. First, the study was limited to animal models, and the therapeutic efficacy of PAA has not yet been validated in clinical settings. Second, while the study demonstrated that PAA activates autophagy via the AMPK/mTOR pathway, the involvement of alternative signaling pathways cannot be excluded and remains to be elucidated. Additionally, the optimal dosing regimen and therapeutic time window for PAA administration have not been fully established, which needs further optimization to enhance its clinical potential. While the use of Compound C highlights the role of the AMPK/mTOR pathway in mediating PAA's cardioprotective effects, its known off-target effects limit the specificity of these findings. To better clarify the AMPK dependency of PAA's effects, future studies should employ more precise and targeted genetic approaches, including siRNA-mediated AMPK knockdown or AMPK knockout mouse models, to determine the underlying mechanisms and confirm PAA as a therapeutic candidate for acute myocardial infarction.

Conclusion

This study offers the first in vivo evidence that PAA promotes autophagy via activation of the AMPK signaling pathway, while simultaneously reducing myocardial inflammation, oxidative stress, and apoptosis in a mouse model of acute myocardial infarction. These results extend previous findings and provide mechanistic insight into the cardioprotective effects of PAA, highlighting its potential as a therapeutic candidate for further exploration in AMI treatment.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Author Contributions

All authors contributed to the study conception and design. Material preparation and the experiments were performed by ZZL. Data collection and analysis were performed by QJ. The first draft of the manuscript was written by JZY. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Ethics Committee of the Affiliated Hospital of Changchun University of Chinese Medicine (Approval No. 2024746).

Acknowledgment

Not applicable.

Funding

Not applicable.

Conflict of Interest

The authors declare no conflict of interest.

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