

Original Article

Cinnamaldehyde attenuates pressure overload-induced cardiac hypertrophy

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Received September 11, 2015; Accepted October 22, 2015; Epub November 1, 2015; Published November 15, 2015

Abstract: Background: Cinnamaldehyde is a major bioactive compound isolated from the leaves of *Cinnamomum osmophloeum*. Studies have demonstrated that cinnamaldehyde has anti-bacterial activity, anti-tumorigenic effect, immunomodulatory effect, anti-fungal activity, anti-oxidative effect, anti-inflammatory and anti-diabetic effect. It has been proven that Cinnamaldehyde improves ischemia/reperfusion injury of pre-treatment. However, little is known about the effect of cinnamaldehyde on cardiac hypertrophy. Methods: Aortic banding (AB) was performed to induce cardiac hypertrophy in mice. Cinnamaldehyde premixed in diets was administered to mice after one week of AB. Echocardiography and catheter-based measurements of hemodynamic parameters were performed at week 7 after starting cinnamaldehyde (8 weeks after surgery). The extent of cardiac hypertrophy was evaluated by pathological and molecular analyses of heart samples. Meanwhile, the effect of cinnamaldehyde on myocardial hypertrophy, fibrosis and dysfunction induced by AB was investigated, as was assessed by heart weight/body weight, lung weight/body weight, heart weight/tibia length, echocardiographic and haemodynamic parameters, histological analysis, and gene expression of hypertrophic and fibrotic markers. Results: Our data demonstrated that echocardiography and catheter-based measurements of hemodynamic parameters at week 7 revealed the amelioration of systolic and diastolic abnormalities by cinnamaldehyde intervention. Cardiac fibrosis in AB mice was also decreased by cinnamaldehyde. Moreover, the beneficial effect of cinnamaldehyde was associated with the normalization in gene expression of hypertrophic and fibrotic markers. Further studies showed that pressure overload significantly induced the activation of extracellular signal-regulated kinase (ERK) signaling pathway, which was blocked by cinnamaldehyde. Conclusion: Cinnamaldehyde may be able to retard the progression of cardiac hypertrophy and fibrosis, probably via blocking ERK signaling pathway.

Keywords: Cinnamaldehyde, cardiac hypertrophy, pressure overload, ERK signaling pathway

Introduction

Cardiac hypertrophy is one of the major causes of morbidity and mortality in the world [1]. It is considered that pathological cardiac hypertrophy is a condition between normal heart and progressively failing heart [2]. Heart failure (HF) is a major health burden accounting for approximately 25% among all deaths in developing countries and HF patients have a mortality of 50% within 4 years [3]. The high mortality of HF may reflect the complex hypertrophic processes leading to HF and the difficulty in reversing cardiac hypertrophy with the available drug therapies [4]. Prevention or reduction of pathological cardiac hypertrophy is an independent goal of treatment, which may serve to prevent or postpone the progression of HF [5]. It has

been demonstrated that the current drug therapies for HF is beneficial for improving life quality of the patients of HF without dramatic reduction of mortality [6]. The future challenge is to hunt for novel pharmacological agents which target the underlying pathophysiological processes, including relevant signaling pathways and cardiac fibrosis, which result in progressive myocardial dysfunction and unfavorable remodeling, thereby ameliorating the long-term outcomes of the patients with HF [7].

Cinnamaldehyde (3-phenyl-prop-2-enal, C₆H₅-CH) is a major bioactive compound which is isolated from the leaves of *Cinnamomum osmophloeum* [8, 9]. Studies have demonstrated that cinnamaldehyde has anti-bacterial activity [8], anti-tumorigenic effect [10],

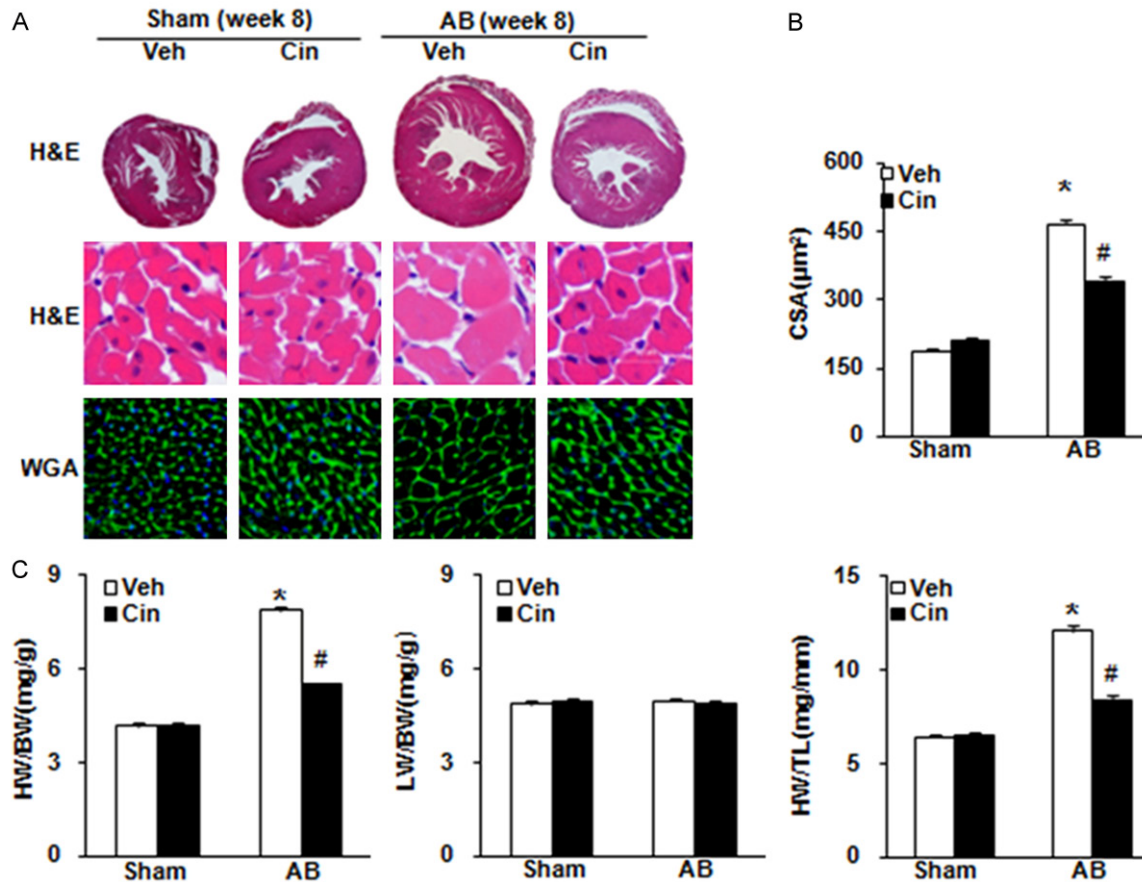


Figure 1. Cinnamaldehyde protected against cardiac hypertrophy. (A) Gross image of the heart, hematoxylin and eosin staining and fluorescein isothiocyanate-labeled wheat germ agglutinin staining of sham and aortic banding (AB) mice at week 8 post surgery (B) Statistical analysis of CSA among the indicated groups. (C) Statistical analysis of HW/BW ratio, LW/BW ratio and HW/TL ratio among the indicated groups. *P<0.05, compared to the corresponding sham group; #P<0.05, compared to AB + vehicle group. Abbreviations: AB, aortic banding; HW/BW, heart weight/body weight; LW/BW, lung weight/body weight; HW/TL, heart weight/tibia length; CSA, myocyte cross-sectional areas.

immunomodulatory effect [11], anti-fungal activity [12], and anti-diabetic effect [13]. Cinnamaldehyde is the main chemical ingredients of Cinnamomum cassia, which has been reported to possess anti-oxidative [14] and anti-inflammatory properties [15]. Aqueous extracts of cinnamon and cinnamon oil have been reported to reduce injury to cardiac function and dynamic change in blood flow induced by isoproterenol (ISO) [16]. Cinnamaldehyde decreases the ST elevation induced by acute myocardial ischemia, decreases serum levels of CK-MB, LDH, TNF- α and IL-6, and increases serum NO activity. Moreover, cinnamaldehyde increases superoxide dismutase (SOD) activity and decreases malondialdehyde (MDA) content in myocardial tissue [17]. Another study showed that Cinnamaldehyde induced endothelium-dependent vasodilation via the Nitric oxide-

cyclic guanosine monophosphate (NO-cGMP) pathway in the rat thoracic aorta [18]. However, the effect of cinnamaldehyde on cardiac hypertrophy and its mechanism are still unclear. In this research, aortic banding (AB) was performed to induce cardiac hypertrophy in mice, and the results showed that cinnamaldehyde may impede the progression of cardiac hypertrophy induced by pressure overload via targeting extracellular signal-regulated kinase (ERK) signaling pathway.

Materials and methods

Chemicals

Cinnamaldehyde (95% purity, which was determined by high-performance liquid chromatography analysis) was bought from Sigma-Aldrich (USA).

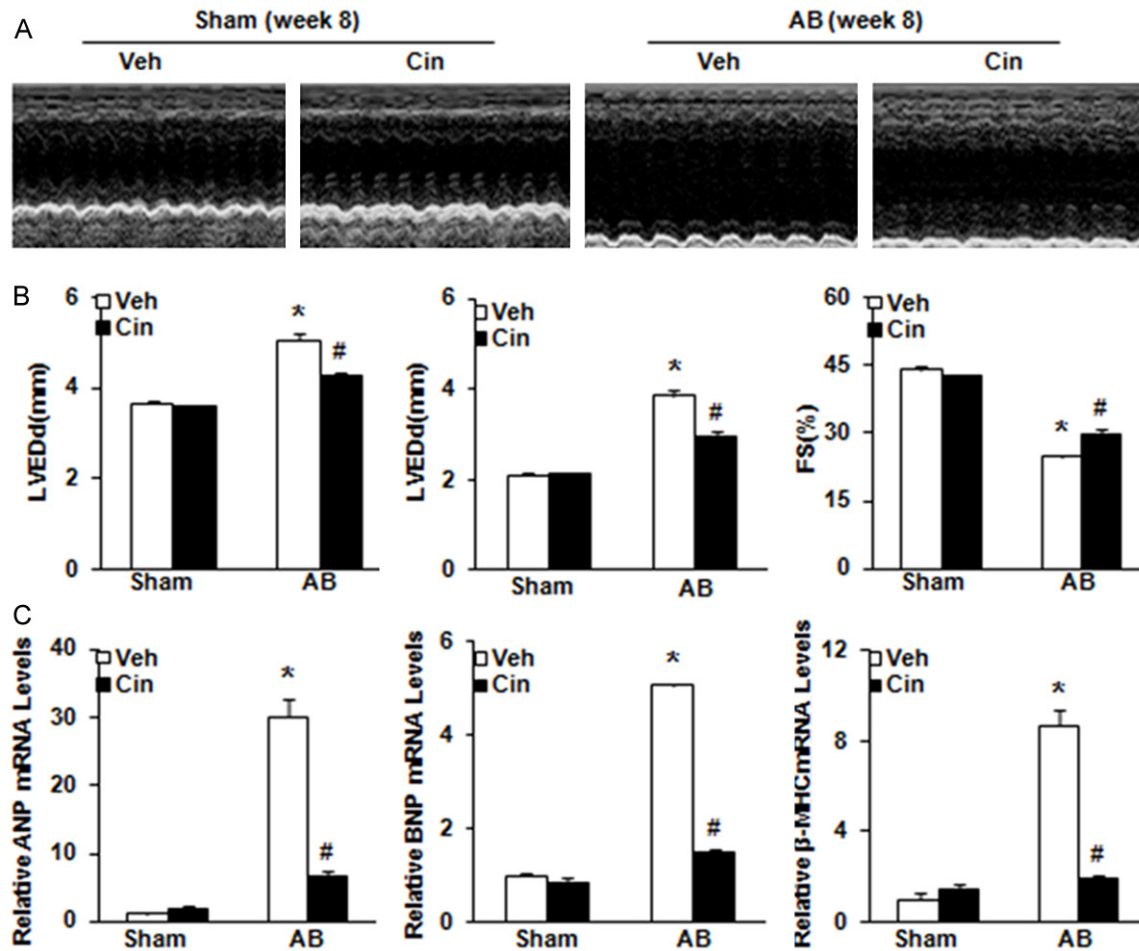


Figure 2. Evidence of attenuation of aortic banding (AB)-induced left ventricular dysfunction by serial echocardiography. A. Representative M-mode images of AB + vehicle and AB + cinnamaldehyde groups. B. Cinnamaldehyde attenuated AB-induced increased left ventricular (LV) diameters including LV end-systolic diameter (LVESd) and LV end-diastolic diameter (LVEDd), and also attenuated AB-induced changes of fractional shortening (FS). Echocardiography was performed at the end of the study (week 8) (n=8). Cinnamaldehyde administration was started from week 1 after AB surgery. C. Expression of transcripts for ANP, BNP and β -MHC which were induced by AB was determined by reverse transcription-polymerase chain reaction (n=8). *P<0.05, compared to the corresponding sham group; #P<0.05, compared to AB + vehicle group. Abbreviations: ANP, atrial natriuretic peptide; BNP, B-type natriuretic peptide; β -MHC, β -myosin heavy polypeptide. *P<0.05, compared to the corresponding sham group; #P<0.05, compared to AB + vehicle group.

Animals

Thirty two male C57/BL6 mice weighing 23.5-27.5 g and aged 8-10 weeks were obtained from Institute of Laboratory Animal Science, CAMS & PUMC (Beijing, China). They were housed under controlled temperature and humidity with a 12-h light-dark cycle, which had free access to food and water in the Cardiovascular Research Institute of Wuhan University (Wuhan, China). The animals were allowed to adapt to the laboratory environment for at least one week, and then randomly assigned to four groups, vehicle-sham group (n=8), cinnamaldehyde-sham group (n=8), vehi-

cle-AB group (n=8) and cinnamaldehyde-AB group (n=8), based on AB and cinnamaldehyde treatment (about 50 mg/kg body weight per day), which began one week after operation and maintained for a further seven weeks. The dose of cinnamaldehyde referred to the literature [19]. The administration of cinnamaldehyde was carried out based on the previous studies [19]. Food consumption was monitored once a week, which was the same among all groups. We conducted AB as described before [20]. Eight weeks after operation, the animals underwent final echocardiography and catheter-based measurements of hemodynamic parameters before sacrifice. The protocols

Table 1. Echocardiographic and hemodynamic parameters in vehicle and cinnamaldehyde (Cin) treated mice 8 weeks after AB surgery

Parameter	Veh-Sham	Cin-Sham	Veh-AB	Cin-AB
Number	8	8	8	8
HR (beats/min)	517.24±13.28	518.17±11.84	523.02±17.93	516.20±21.64
IVSd (mm)	0.68±0.05	0.65±0.07	0.87±0.10*	0.72±0.07#
LVEDd (mm)	3.65±0.13	3.59±0.12	5.06±0.44*	4.25±0.021#
LVPWd (mm)	0.68±0.04	0.66±0.05	0.87±0.11*	0.73±0.08#
IVSs (mm)	1.04±0.16	1.05±0.12	1.36±0.10*	1.18±0.15*
LVESd (mm)	2.09±0.20	2.11±0.12	3.6±0.27*	3.06±0.11#
LVPWs (mm)	1.05±0.08	1.05±0.07	1.42±0.11*	1.19±0.16#
LVEF (%)	80.38±2.74	80.41±1.93	56.69±2.23*	61.78±4.23#
FS (%)	43.93±1.91	42.34±1.72	24.76±1.07*	29.80±2.06#
ESP (mmHg)	109.33±9.72	106.66±5.5	143.13±4.87*	146.77±4.11*
dP/dTmax (mmHg/s)	10564±273	10649±413	7728±281*	9036±347#
dP/dTmin (mmHg/s)	-9331±350	-9431±254	-7117±473*	-8722±268#

Data are expressed as mean ± SEM. *P<0.05, compared to Vehicle-sham group; #P<0.05, compared to Vehicle-AB group. Veh-Sham, vehicle-sham; Cin-Sham, cinnamaldehyde-sham; Veh-AB, vehicle-aortic banding; Cin-AB, cinnamaldehyde-aortic banding; HR, heart rate; IVSd, end-diastolic ventricular septal thickness; LVEDd, left ventricular end-diastolic diameter; LVPWd, left ventricular posterior wall thickness; IVSs, interventricular septal thickness at end-systole; LVESd, end-systolic diameter; LVPWs, left ventricular posterior wall thickness at end-systole; LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; ESP, end-systolic pressure; dP/dt min, minimal rate of pressure decay; dP/dt max, maximal rate of pressure development.

Table 2. General data in vehicle and cinnamaldehyde (Cin) treated mice after 8 weeks of AB surgery

Parameter	Veh-Sham	Cin-Sham	Veh-AB	Cin-AB
Number	8	8	8	8
BM (g)	28.96±0.89	28.77±0.74	28.62±0.76	28.39±0.54
HW (mg)	120.78±3.13	120.78±3.31	226.23±6.53*	156.38±3.66#
LW (mg)	140.60±2.43	143.54±4.54	144.47±3.20	138.41±2.67
HW/BM (mg/g)	4.16±0.12	4.20±0.08	7.90±0.14*	5.52±0.07#
LW/BM (mg/g)	4.86±0.12	4.99±0.11	4.97±0.09	4.87±0.10
HW/TL (mg/mm)	6.43±0.13	6.50±0.18	12.10±0.36*	8.42±0.25#

Data are expressed as mean ± SEM. *P<0.05, compared to Vehicle-sham group; #P<0.05, compared to Vehicle-AB group. Veh-Sham, vehicle-sham; Cin-Sham, cinnamaldehyde-sham; Veh-AB, vehicle-aortic banding; Cin-AB, cinnamaldehyde-aortic banding; BM, body mass; HW, heart weight; LW, lung weight; HW/BM, heart weight/body weight; LW/BM, lung weight/body weight; HW/TL, heart weight/tibial length.

were approved by Institutional Guidelines of the Animal Care and Use Committee of Renmin Hospital of Wuhan University, conforming to the Guide for the Care of Laboratory Animals published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1996). All operation and analyses were performed blindly for all groups.

Echocardiography

Echocardiographic analyses were carried out 8 weeks after operation. Echocardiography was conducted in anesthetized (1.5% isoflurane) mice using a Mylab 30CV (Esaote S.P.A, Genoa,

Italy), which was equipped by a 10-MHz linear array ultrasound transducer. We evaluated the left ventricle (LV) dimensions in parasternal short-axis view during systole or diastole, and measured LV end-diastolic diameter (LVEDd), LV end-systolic diameter (LVESd), left ventricular posterior wall thickness (LVPWd) and end-diastolic ventricular septal thickness (IVSd) from the LV M-mode tracing with a sweep speed of 50 mm/s at the mid-papillary muscle level.

Catheter-based measurements of hemodynamic parameters

For the purpose of hemodynamic measurements, mice were anesthetized by 1.5% isoflurane, and a microtip catheter transducer (SPR-839, Millar Instruments, Houston, TX, USA) was inserted into the left ventricle through the right carotid artery. The signals were recorded using a Millar Pressure-Volume System (MPVS-400, Millar Instruments), and the PVAN data analysis software (Millar Instruments) was

employed to analyze the heart rate (HR), end-systolic pressure (ESP), end-diastolic pressure (EDP), minimal rate of pressure decay (dP/dt min) and maximal rate of pressure development (dP/dt max).

Histological analysis

The heart was removed, and arrested in diastole with 10% KCl. Then it was weighed, fixed with 10% formalin, and embedded in paraffin. The heart was cut transversely close to the apex so as to visualize the left and right ventricle. Sections were 4-5 µm thin and mounted

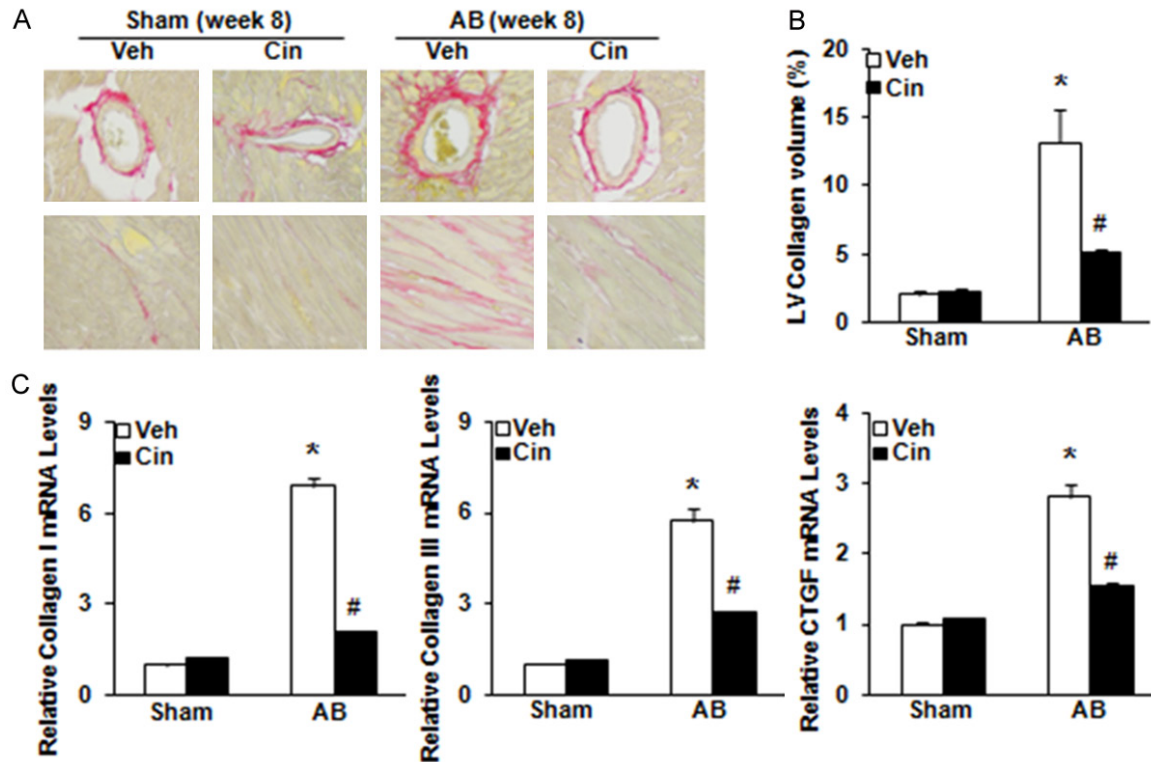


Figure 3. Cinnamaldehyde alleviated fibrosis of the pressure-overload heart. A. The histological section of left ventricle in the indicated group was stained by picrosirius red. B. Fibrotic areas in the histological section were quantified by an image-analysis system. C. mRNA expression of collagen I α , collagen III, and CTGF in the myocardium from the indicated groups was determined by reverse transcription-polymerase chain reaction. * $P < 0.05$, compared to the corresponding sham group; # $P < 0.05$, compared to AB + vehicle group. Abbreviations: AB, aortic banding. CTGF, connective tissue growth factor.

onto slides. For histological analysis, picrosirius red (PSR) staining and hematoxylin and eosin (H&E) staining were employed. Tissue sections were observed under a light microscopy. The sections were stained for myocyte cross-sectional area with fluorescein isothiocyanate-labeled wheat germ agglutinin (Invitrogen, Carlsbad, CA, USA) and 4',6-diamidino-2-phenyl-indole (DAPI) to visualize membranes and nuclei. A single myocyte was analyzed with a quantitative digital image analysis system (Image Pro-Plus, version 6.0; Media Cybernetics, Bethesda, MD, USA). One hundred to two hundred myocytes in the left ventricle were outlined in each group.

Quantitative real-time reverse transcription-polymerase chain reaction

In order to determine the relative mRNA expression of atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), collagen I, collagen III, β -myosin heavy polypeptide (β -MHC), and

connective tissue growth factor (CTGF), TRIzol (Invitrogen, 15596-026) was used to collect RNA from LV tissue, which was then reversely transcribed into cDNA for real-time polymerase chain reaction (PCR) analysis using the Transcriptor First Strand cDNA Synthesis Kit (04896866001, Roche, Basel, Switzerland) and oligo (DT) primers. A Light Cycler 480 SYBR Green 1 Master Mix (Roche, 04707516001) was used for quantification of the PCR amplification, and the results were normalized against glyceraldehyde-3-phosphatedehydrogenase (GAPDH) gene expression.

Western blotting

Protein levels from all samples were evaluated using the BCA-kit (23227, Thermo Fisher Scientific, Waltham, MA, USA) followed by normalization of protein concentration before the subsequent procedures. Sodium dodecyl sulphate polyacrylamide gel electrophoresis was used to separate protein samples (50 μ g),

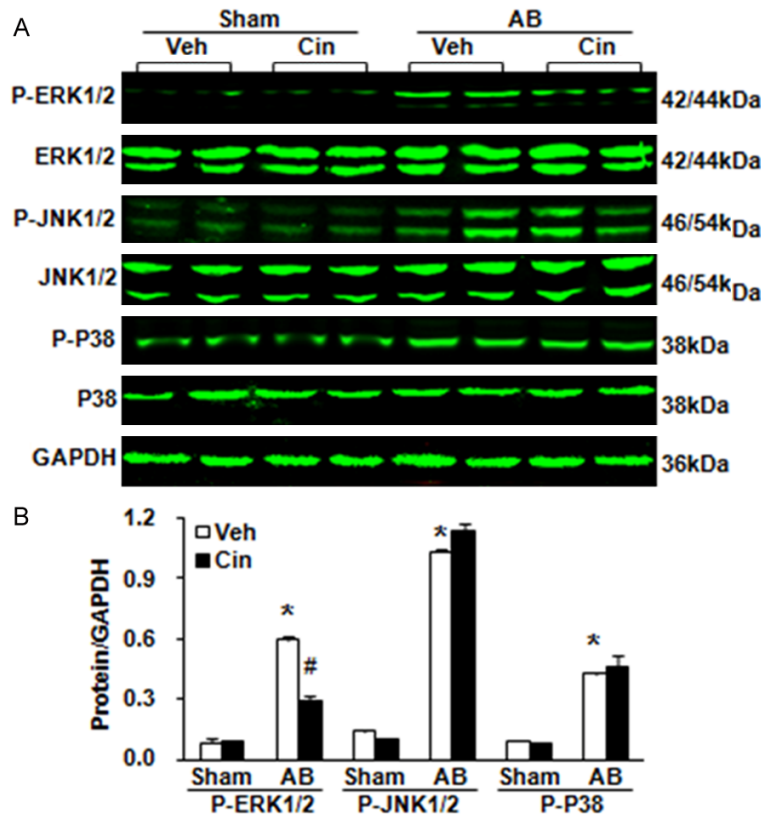


Figure 4. Effect of cinnamaldehyde on JNK signaling pathway. A, B. MAPK expression was determined by Western blot. A. Representative blots of P-ERK1/2, P-JNK1/2 and P-p38 in the heart tissues of mice among the indicated groups (n=8). B. Quantitative results. *P<0.05, compared to the corresponding sham group; #P<0.05, compared to AB + vehicle group. Abbreviations: JNK, c-Jun N-terminal kinase; MAPK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinase; AB, aortic banding; GAPDH, glyceraldehyde-3-phosphate dehydrogenase.

which were then transferred to immobilon-FL transfer membrane (IPFL00010, Millipore, Billerica, MA, USA). The membrane was blocked with 5% milk in Tris-buffered saline Tween-20 (TBST) for 3 h, which was then incubated overnight with the indicated primary antibodies under 4°C. Antibodies against phospho-extracellular signal-regulated kinase(ERK)1/2^{Thr202/Tyr204}(#4370), ERK1/2 (#4695), phospho-p38^{Thr180/Tyr182}(#4511), p38(#9212), phospho-JNK1/2^{Thr183/Tyr185}(#4668) and JNK1/2(#9285) were bought from Cell Signaling Technology (Danvers, MA, USA). The antibody against GAPDH (MB001) was purchased from Bioworld Technology, St Paul, MN, USA. The blots were scanned by a two-color infrared imaging system (Odyssey, LI-COR, Lincoln, NE, USA), and expression levels of the specific protein were normalized to GAPDH protein for total cell lysates.

Statistical analysis

SPSS 19.0 software was used for statistical analysis. The data were expressed as the mean ± SEM. One-way ANOVA test and post hoc Tukey test were employed for data analysis. P<0.05 indicated significant difference.

Results

Cinnamaldehyde protected against cardiac hypertrophy

Whether the index of cardiac hypertrophy and heart failure was attenuated by cinnamaldehyde administration which began from 1 week following AB surgery was determined. Compared to the sham group, mice which underwent AB surgery showed noticeable cardiac hypertrophy at the end of 8 weeks, as was indicated by increased cardiac mass, heart weight/body weight (HW/BW), myocyte cross sectional area (CSA), heart weight/tibial length (HW/TL) (Figure 1 and Table 2). However, these hypertrophic responses were attenuated by 7-week admin-

istration of cinnamaldehyde (Figure 1). The induction of hypertrophic markers 8 weeks after AB surgery, including ANP, BNP and β-MHC, was also significantly blunted in mice treated by cinnamaldehyde (Figure 2C).

Cinnamaldehyde improved the impaired cardiac function after AB

The effect of cinnamaldehyde on AB-induced left ventricular dysfunction was evaluated by echocardiography 8 weeks after operation. As shown in Table 1 and Figure 2, 8 weeks after AB, chamber diameter was significantly increased and left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (FS) were depressed. Cardiac dilation and left ventricular function improvement were caused by Cinnamaldehyde administration. Catheter-based hemodynamic measurement was con-

ducted 8 weeks after AB so as to further evaluate left ventricular systolic and diastolic function. AB led to significant increase of diastolic blood pressure and decrease of systolic function and diastolic function. The animals which were treated by cinnamaldehyde showed normalization of the hemodynamic parameters, including EDP, dP/dt max, and dP/dt min (**Table 1**). No significant differences of HR were found between the groups.

Cinnamaldehyde attenuated pressure overload-induced cardiac fibrosis

Fibrosis is integral characteristics of LV hypertrophy and HF. The heart tissue section was PSR stained to detect the development of interstitial fibrosis in mice of each group. We observed obvious interstitial fibrosis in mice which were subjected to AB surgery, and it was attenuated by cinnamaldehyde (**Figure 3A** and **3B**). The changes of myocardial pro-fibrotic genes expression were also examined. As revealed in **Figure 3C**, the expression of collagen I α , collagen III and CTGF induced by pressure overload was normalized by cinnamaldehyde.

Cinnamaldehyde inhibited the activation of ERK1/2 signaling pathway after AB

The above results suggest that cinnamaldehyde might suppress pressure overload-induced cardiac hypertrophy. However, the underlying mechanism by which cinnamaldehyde regulates the hypertrophic response remains unknown. Given that the mitogen-activated protein kinase (MAPK) signaling pathway has been previously shown to play an important role in cardiac hypertrophy, we first examined whether cinnamaldehyde affected the AB-induced MAPK signaling response. As expected, we observed that ERK1/2, c-Jun N-terminal kinase 1/2 (JNK1/2), and p38 were significantly phosphorylated in AB mice. However, the phosphorylation of ERK1/2 was almost completely inhibited in the cinnamaldehyde-treated hearts compared with the vehicle-treated hearts, whereas JNK1/2 and p38 were not significantly affected (**Figure 4A** and **4B**). These data suggest that the regulation of cinnamaldehyde in hypertrophy might be mediated by ERK1/2 signaling pathway.

Discussion

Previous studies have supported the traditional use of *Cinnamomum cassia* which has anti-oxi-

dative [21], anti-inflammatory [22], anti-thrombotic [23] and anticancer [24] properties. *Cinnamomum cassia* has potential therapeutic benefits in cardiovascular disease. Aqueous extracts of *Cinnamomum cassia* have been reported to reduce injury of cardiac function and dynamic change in blood flow induced by isoproterenol (ISO) [25]. Cinnamaldehyde is a pure extract and the major bioactive component of *Cinnamomum cassia* [26]. In this study, it was found that 8 weeks after AB, mice developed cardiac hypertrophy and fibrosis characterized by increase of HW/BW ratio, HW/TL ratio, cross-section area of cardiomyocytes, collagen accumulation, expression of hypertrophic and fibrotic markers in myocardium, leading to LV related dilation and dysfunction. Cinnamaldehyde retarded the development of cardiac hypertrophy and fibrosis in mice which were subjected to pressure overload associated with the regulation on the ERK pathway.

Much of the recent work has focused on the anti-oxidative [27] and anti-inflammatory [28] activities of cinnamaldehyde. In the kidney, cinnamaldehyde decreases the level of non-enzymatic antioxidants and increases the activity of antioxidant enzymes [29]. The compound also possesses antidiabetic properties in the rat [30], which can reduce visceral fat deposition in mice fed with high-fat and high-sucrose diet [31]. Cinnamaldehyde prevents development of hypertension in insulin deficiency and insulin resistance through normalization of vascular contractility in addition to its insulinotropic effect in insulin deficiency [32]. With regard to acute cardiovascular effects, cinnamaldehyde reduces peripheral resistance, lowers arterial blood pressure in dogs [33] and rats [34], and increases hind paw blood flow in mice [35]. However, in the latter species, a single dose of cinnamaldehyde causes biphasic changes in arterial blood pressure, with an initial drop followed by a pressor response [35]. In vitro, relaxation of rat aortae [36] and mouse mesenteric arteries [35] is induced by cinnamaldehyde. Chronic treatment (6 weeks) with cinnamaldehyde protects against increase of diastolic blood pressure after induction of diabetes in Wistar rats [36, 37]. As the major bioactive component of *Cinnamomum cassia*, cinnamaldehyde has been proven to improve ischemia/reperfusion injury before treatment [38, 39]. Cinnamaldehyde shows cardioprotective effect in a rat model of ischemic myocardial injury,

which is attributed to anti-oxidative and anti-inflammatory properties as well as increased NO [40]. It is reported that after cinnamaldehyde treatment of renal interstitial fibroblasts that have been stimulated by high glucose, their ability of proliferation and hypertrophy is reduced through mechanism that may be dependent on inactivation of the ERK/JNK/p38 MAPK pathway [41]. However, it is not clear whether cinnamaldehyde can retard the process of cardiac hypertrophy. Accordingly, our study addresses the potential of cinnamaldehyde in protecting against cardiac hypertrophy in mice subjected to pressure overload.

The possible mechanisms by which cinnamaldehyde regulates cardiac hypertrophy remain unclear. It is generally accepted that biomechanical stress induced by pressure overload triggers a variety of signal transduction molecules and pathways that regulate the hypertrophic growth of cardiac myocytes. Numerous studies have demonstrated that the MAPK signaling pathway plays a critical role in the pathogenesis of cardiac hypertrophy and heart failure. The MAPK cascade comprises a sequence of successive kinases, including ERKs, JNKs, and p38, which is triggered in cardiac myocytes by stress stimuli. After this cascade is activated, ERKs, JNKs, and p38 phosphorylate a wide array of intracellular targets, resulting in the reprogramming of cardiac gene expression [42-45]. To examine the molecular mechanisms involved in the ability of cinnamaldehyde to regulate cardiac hypertrophy, we investigated the activation status of the MAPK pathway in our hypertrophic models. It was found that the activation of ERK1/2 was blocked by the treatment of cinnamaldehyde. However, the treatment of cinnamaldehyde did not affect the phosphorylation of JNK1/2 and p38. These findings suggested that the protective role of cinnamaldehyde in pathological cardiac hypertrophy was at least partially mediated via the ERK1/2 signaling pathway. However, further experiments are needed to determine the molecular mechanism by which cinnamaldehyde regulates the ERK1/2 pathway.

Cardiac fibrosis is an additional classic feature of pathological hypertrophy, which is characterized by the expansion of the extracellular matrix caused by collagen accumulation [46, 47]. Our study demonstrated that cinnamaldehyde ablation significantly inhibited cardiac fibrosis and attenuated the expression of several fibrotic

mediators induced by chronic pressure overload. These findings suggested that the protective role of cinnamaldehyde in pathological cardiac hypertrophy was dependent, at least partly associated with the protective of cardiac fibrosis.

In conclusion, this study is the first one to define a role of cinnamaldehyde in cardiac hypertrophy. Our findings indicated that the treatment of cinnamaldehyde mitigated the development of pathological cardiac hypertrophy and heart failure. The mechanism underlying the protective role of cinnamaldehyde in the development of cardiac hypertrophy seemed to be related to the ERK1/2 signaling pathway. These findings provide novel insights into the molecular mechanisms underlying pathological cardiac hypertrophy. Based on these findings, cinnamaldehyde might represent a new therapeutic target for suppressing the onset of cardiac hypertrophy and failure.

Acknowledgements

This research was supported by the National Natural Science Foundation of China (810-00036 and 81000095) and the Fundamental Research Funds for the Central Universities of China (2012302020212 and 2012302020-211).

Disclosure of conflict of interest

None.

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