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# Beneficial effects of the extract from *Corydalis yanhusuo* in rats with heart failure following myocardial infarction

Limao Wu, Haiyun Ling, Lianda Li, Lianxiu Jiang and Minle He

## Abstract

As indicated in ancient Chinese medical books, *Corydalis yanhusuo* has therapeutic effects on cardiovascular diseases. The analgesic effect of this plant has been fully elucidated, and l-tetrahydropalmatine has been shown to be the main active principle. The aim of this investigation was to evaluate its protective effects in a rat heart failure model. Rats were subjected to coronary artery ligation, and orally administered with ethanolic extract of *Corydalis yanhusuo* 50, 100, or 200 mg $kg^{-1}$ daily, from the 7th day after surgery. We measured cardiac function, plasma atrial natriuretic peptide (ANP), relative heart and lung weights, infarct size and ventricular dilatation after treatment for 8 weeks. Administration with *Corydalis yanhusuo* led to a significant reduction in infarct size and improvement in cardiac function as demonstrated by lower left ventricular end diastolic pressure (LVEDP) and elevated $\pm dp/dt_{max}$. We also found that *Corydalis yanhusuo* significantly reduced left ventricular (LV)/body weight ratio, lung/body weight ratio and significantly inhibited neurohormonal activation. Taken together, this study indicated that *Corydalis yanhusuo* exerted salutary effects on heart failure induced by myocardial infarction in rats.

## Introduction

Heart failure is a syndrome characterized by impaired cardiac function, decreased exercise tolerance and quality of life and high morbidity and mortality. Heart failure indicates a chronic disorder in which the heart's diminished ability to pump blood effectively leads to reduced blood flow, back-up pressure of blood in the veins and lungs and other changes that may further weaken the heart. Coronary heart disease remains the most prominent cause of heart failure (Baicu et al 2005). Myocardial infarction (MI) leads to cardiac dysfunction via an initial loss of myocardium and then a subsequent remodelling of the left ventricle. This remodelling process results in the expansion of the border zone of myocardium along the infarct, progressive left ventricular (LV) dilation, fibrosis, wall thinning and, ultimately, further loss of function and the clinical syndromes of heart failure (Freudenberger et al 2006; Jankowska et al 2006; van Heerebeek et al 2006). Although angiotensin-converting enzyme inhibitors improve haemodynamic profiles and survival times and prevent cardiac dilation in animals and patients with congestive heart failure following MI (Mann & Bristow 2005; Inglis et al 2006), current therapy for heart failure is still far from optimal.

*Corydalis yanhusuo* W.T., a perennial herb belonging to the Papaveraceae family, has been used in traditional herbal remedies in China, Japan and Korea. *Corydalis yanhusuo* grows wild in Siberia and Northern China and is cultivated principally in the Zhejiang province of China. The dried and pulverized tuber of *Corydalis yanhusuo* is also called *Rhizoma Corydalis* or *Yanhusuo*. In traditional Chinese medicine, it has been used for hundreds of years to help invigorate the blood, dispel stasis and moving *qi*, reinforce vital energy and alleviate painful conditions, such as headache, chest pain, hypochondriac pain and trauma, especially angina pectoris (Ma 1983; Ding 1987; Yuan et al 2004). The main active components isolated from *Corydalis yanhusuo* are alkaloids (Ma & Chen 1985; Fu et al 1986a, b). Those alkaloids have been proved to possess beneficial effects in heart disease (Ma et al 1986; Liu & Zhao 1987; Xuan et al 1992; Xing et al 1994; Lin et al 1996; Huang et al 1999).

Department of Pharmacology, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou 310058, P R China

Limao Wu, Haiyun Ling, Lianda Li, Lianxiu Jiang, Minle He

**Correspondence:** L. Wu, Department of Pharmacology of TCM, College of Pharmaceutical Science, Zijingang Campus, Zhejiang University, Hangzhou, 310058, P. R. China. E-mail: wulimao@yahoo.com.cn

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In recent years, medicinal herbs and their extracts have received great attention for their salutary effects in heart failure (Valli & Giardina 2002; Yeh et al 2006). This investigation was prompted by the claim of Chinese traditional healers that patients who took the extract from C*orydalis yanhusuo* as a modulator for heart failure had their syndromes markedly relieved. However, to the best of our knowledge, there is no report about the cardioprotection of *Corydalis yanhusuo* on animal heart failure models. Therefore, the aim of this study was to investigate the effect of *Corydalis yanhusuo* on heart failure induced by coronary occlusion in rats with the purpose of identifying a simple, cheap, safe, effective and easily accessible source of natural remedy for the treatment of heart failure.

## Materials and Methods

### Plant materials

The rhizome of *Corydalis yanhusuo* W.T. was supplied by Xi'an Sanjiang Bio-Engineering Co., Ltd. The species of medicinal herb were identified by Professor Jinxiang Yang, Northwest Institute of Botany, Chinese Academy of Sciences. Voucher specimens were deposited at the Herbarium, laboratory of Pharmacology on Traditional Chinese Medicine of Zhejiang University, CHN.

### Extraction

The rhizome of *Corydalis yanhusuo* was cut into small pieces, powdered and then extracted by 85% alcohol three times. After retrieving the alcohol, the extract was freeze-dried, finally giving a powdery, crude extract of *Corydalis yanhusuo*. Further chemical analysis was performed with a Waters 2695 HPLC system. Briefly, analytical conditions were as follows. The analytical column was a Zorbax SB-C18 (5 $\mu$m, 4.6×250 mm) with a Zorbax SB-C18 (5 $\mu$m, 4.6×45 mm) guard column (both from Agilent Technologies). The eluents consisted of A (3.7 mM phosphoric acid buffer, pH 2.55) and B (100% acetonitrile). The condition was set at 30% of B (Fu et al 1986a, b).

### Preparation of heart failure rats and experimental protocol

All animals received humane care in compliance with the standards established by the Guide for the Care and Use of Laboratory Animals of Zhejiang University. Post-infarction heart failure was induced by ligation of the left coronary artery in rats. Briefly, male Sprague-Dawley rats, 180 ± 20 g, underwent left thoracotomy under sodium pentobarbital (45 mg kg$^{-1}$, i.p.) anaesthesia. The incised area was extended using forceps and the pericardium was opened. The heart was then pushed out of the chest and the left anterior descending coronary artery was ligated using silk thread. Successful ligation was verified by the occurrence of arrhythmias and, visually, by the colour change of the ischaemic area. The heart was immediately returned to its anatomical position and the chest was closed while slight pressure was applied from outside so that air did not remain in the chest. The skin was then sutured using wound clips. Sham-operated rats underwent the same surgical operation without actual coronary ligation. In this study, mortality within 1 week of the operation was approximately 20%. After 1 week, rats were distributed into 6 groups. In the vehicle control group (n = 16), rats were orally given physiologic saline as vehicle at a dose of 10 mL kg$^{-1}$. In the captopril 50 mg kg$^{-1}$ group (n = 15), rats were orally given captopril 50 mg kg$^{-1}$. In the *Corydalis yanhusuo* 200 mg kg$^{-1}$, 100 mg kg$^{-1}$ and 50 mg kg$^{-1}$ groups (n = 13 each), rats were orally given the extract from *Corydalis yanhusuo* at a dose of 200, 100 or 50 mg kg$^{-1}$, respectively. In the sham group (n = 13), rats were orally given physiologic saline at a dose of 10 mL kg$^{-1}$. Rats were housed in makrolon cages (5 rats per cage) and maintained in our laboratory in air-conditioned animal quarters with a 12-h light–dark cycle. Rats were dosed once a day for 8 consecutive weeks, then haemodynamic, morphological and plasma biochemical parameters were measured.

### Measurement of haemodynamic parameters

Eight weeks after the beginning of treatment, rats were anaesthetized with sodium pentobarbital (45 mg kg$^{-1}$, i.p.). A catheter was inserted via the right carotid artery into the left ventricle. When a stable and reproducible pressure reading was obtained, the haemodynamic measurements of left ventricular end-diastolic pressure (LVEDP) and the peak rate of rise of left ventricular pressure (±dp/dt) were measured with a pressure transducer and a differentiator (Medease Science and Technology Co., Ltd, Nanjing, China).

### Measurement of plasma atrial natriuretic peptide (ANP) level

A PE-50 catheter was inserted into the right carotid artery after the haemodynamic measurements, and 2 mL blood was collected from the catheter into ice-cooled tubes with 70 $\mu$g mL$^{-1}$ of aprotinin and 1.5 mg mL$^{-1}$ of ethylenediamine tetraacetic acid (EDTA) 2 Na. The blood was centrifuged immediately at 4°C and the plasma was stored at −80°C until the assay of ANP. According to the supplier' instructions, the ANP concentration was measured with an ANP radioimmunoassay kit (Kemeidongya Biotechnologies Co., Ltd, Beijing, China).

### Measurement of relative heart and lung weights

After obtaining haemodynamic measurements, the rat was sacrificed and the lung and heart removed. The heart was dissected into two sections: left ventricle, including the interventricular septum, and right ventricle. The tissues were rinsed with ice-cold saline, blotted and weighed. Relative values (organ weight/body weight) were used in the evaluation. The ratio of the wet-to-dry weight (oven at 45°C for 24 h) of the lungs was taken as a parameter for pulmonary oedema.

### Measurement of infarct size and ventricular dilatation

Infarct size was measured in the same paraffin sections as those used for histological assessment. The excised hearts

were cut into four transverse slices and embedded in paraffin so that the four slice levels appeared on the slides. Typically, the apex slice and the second (and often third) slice of the apical side contained transverse sections of the infarct. The apex slice always had full circumferential infarction. The images of the section were captured and digitalized, and then the area and the length of infarct were measured in all of the four slices using Image C Morphology analysis system (Chansan, Shanghai, China). The infarct size was expressed as a ratio of the sum of infarct area relative to the entire left ventricular area. The infarcted myocardium was identified by histology and staining of scar tissue. Infarct size was also estimated by infarct length as previously described (Fuchs et al 2003). Infarct length was measured along the endocardial and epicardial surface in each of the transverse cardiac sections, and values from all specimens were summed. Infarct length (as a percentage) was calculated as infarct circumference divided by total cardiac circumference. The surgery to induce MI was performed by a single investigator.

Infarct length (IL), circumference and inner diameter of the left ventricle (LVC and LVD, respectively) of the transsection were also calculated according to the following formulae: IL (cm) = (endocardial + epicardial infarct length) × ½; LVC (cm) = (endocardial + epicardial length of the left ventricle) × ½; LVD (cm) = endocardial circumference /$\pi$.

### Statistical analysis

All data were expressed as mean ± s.d. Database was set up with SPSS 12.0 software package (SPSS Inc., Chicago, IL). Differences among groups were analysed by one-way analysis of variance. A Dunnett's post-hoc was used for comparison of each treatment group with the corresponding vehicle control. $P < 0.05$ was considered statistically significant.

## Results

### Chemical composition of the constituents of alkaloids of *Corydalis yanhusuo* extract

A lot of alkaloids were identified from the extract of the rhizome of *Corydalis yanhusuo*, including tetrahydropalmatine, palmatine, dehydrocorydaline, protopine and other alkaloids (Figure 1). The content of *dl*-tetrahydropalmatine (*dl*-THP) in the resultant extract was 15.70% and dehydrocorydaline (DHC) was 1.28% detected by HPLC.

### Effect of *Corydalis yanhusuo* on haemodynamic parameters of rats

Cardiac function in heart failure, with or without *Corydalis yanhusuo* treatment, is shown in Table 1. Peak left ventricular +dp/dt, and peak left ventricular −dp/dt decreased significantly and left ventricular end-diastolic pressure (LVEDP) increased significantly in heart-failure control rats compared with the values for the sham rats. In *Corydalis yanhusuo*-treated heart failure rats, left ventricular end-diastolic pressure was significantly decreased at 9 weeks from 19 ± 5 mmHg (heart failure) to 12 ± 2 mmHg (*Corydalis yanhusuo*, 100 mg kg$^{-1}$) and to 9 ± 3 mmHg (*Corydalis yanhusuo*, 200 mg kg$^{-1}$). *Corydalis yanhusuo* at 100 and 200 mg kg$^{-1}$ daily improved peak left ventricular ±dp/dt significantly.

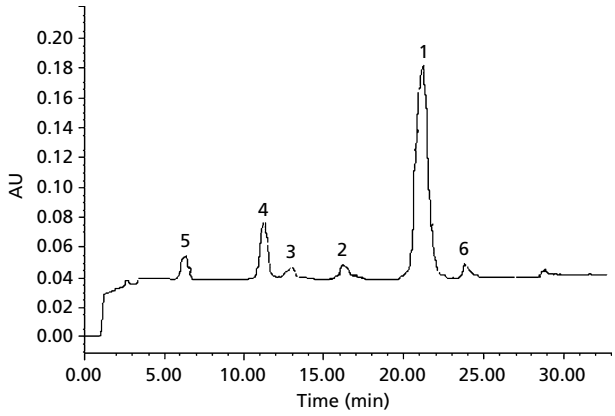


**Figure 1** A typical HPLC chromatogram of the extract from *Corydalis yanhusuo*. Peak 1, tetrahydropalmatine; peak 2, dehydrocordaline; peak 3, palmatine; peak 6, protopine; peaks 4 and 5, unknown constituents.

### Effect of *Corydalis yanhusuo* on plasma atrial natriuretic peptide (ANP) activity

The plasma activity of ANP was increased in the vehicle control group compared with the sham group of rats. Administration with *Corydalis yanhusuo* 200, 100 and 50 mg kg$^{-1}$ resulted in a dose-dependent reduction in plasma ANP levels. There was significant difference between the *Corydalis yanhusuo* 200 mg kg$^{-1}$ group and vehicle control group (Table 1).

### Effect of *Corydalis yanhusuo* on relative heart and lung weight

Induction of large MIs led to a significant cardiac hypertrophy with increased weights of both ventricles normalized to the body weight. Oral administration of *Corydalis yanhusuo* (200 mg kg$^{-1}$) caused a significant decrease in right ventricular and lung weight at 8 weeks, and *Corydalis yanhusuo* was more effective at 200 mg kg$^{-1}$ than at 100 mg kg$^{-1}$ or 50 mg kg$^{-1}$. As a sign of chronic heart failure, the ratio of the wet-to-dry weight of the lungs was significantly increased after large MI. Chronic treatment with *Corydalis yanhusuo* had great effect on these parameters compared with vehicle control (Table 2).

### Effect of *Corydalis yanhusuo* on infarct size and ventricular dilatation

The infarct area was approximately 38% of the left ventricle in the vehicle control rats. Treatment with *Corydalis yanhusuo* (200 mg kg$^{-1}$) significantly reduced the infarct size of the left ventricle compared with vehicle control (32.28 ± 5.68% vs 38.39 ± 7.26%, $P < 0.05$). Infarct size was also reduced with the *Corydalis yanhusuo* treatment at 100 mg kg$^{-1}$ and

**Table 1** Effect of *Corydalis yanhusuo* on haemodynamic parameters and plasma ANP level in heart failure rats

| Group | Dose (mg kg$^{-1}$) | Rat No. | LVEDP (mmHg) | +dp/dtmax (mmHg s$^{-1}$) | –dp/dtmax (mmHg s$^{-1}$) | ANP (pg mL$^{-1}$) |
|---|---|---|---|---|---|---|
| Sham | — | 13 | 4 ± 2 | 11 885 ± 1410 | –8335 ± 1984 | 298 ± 105 |
| Vehicle | — | 16 | 19 ± 5 | 4407 ± 887 | –3173 ± 631 | 1354 ± 899 |
| Captopril | 50 | 15 | 9 ± 2** | 8104 ± 946** | –5470 ± 1316** | 695 ± 294* |
| *Corydalis* | 50 | 13 | 15 ± 5 | 4967 ± 554 | –3665 ± 758 | 1254 ± 877 |
| | 100 | 13 | 12 ± 2** | 5873 ± 842** | –4369 ± 795** | 949 ± 624 |
| | 200 | 13 | 9 ± 3** | 8001 ± 766** | –5146 ± 816** | 718 ± 329* |

LVEDP, left ventricular end diastolic pressure; ±dp/dt, change in left ventricular pressure; ANP, atrial natriuretic peptide. All data are expressed as mean ± s.d. *$P < 0.05$, **$P < 0.01$ vs vehicle control group.

**Table 2** Effect of *Corydalis yanhusuo* on relative heart and lung weight and lung wet/dry weight ratio in heart failure rats

| Group | Dose (mg kg$^{-1}$) | Rat No. | LVW/BW (mg g$^{-1}$) | RVW/BW (mg g$^{-1}$) | THW/BW (mg g$^{-1}$) | LW/BW (g/100 g) | Lung wet/dry weight ratio |
|---|---|---|---|---|---|---|---|
| Sham | — | 13 | 1.87 ± 0.33 | 0.51 ± 0.13 | 2.84 ± 0.55 | 0.57 ± 0.13 | 4.14 ± 0.63 |
| Vehicle | — | 16 | 2.37 ± 0.29 | 0.72 ± 0.09 | 3.68 ± 0.48 | 1.00 ± 0.35 | 5.67 ± 1.71 |
| Captopril | 50 | 15 | 2.03 ± 0.38** | 0.54 ± 0.11** | 3.12 ± 0.52** | 0.71 ± 0.21** | 4.47 ± 1.42* |
| *Corydalis* | 50 | 13 | 2.39 ± 0.38 | 0.67 ± 0.18 | 3.56 ± 0.37 | 0.89 ± 0.28 | 5.10 ± 1.16 |
| | 100 | 13 | 2.21 ± 0.34 | 0.60 ± 0.11** | 3.39 ± 0.47 | 0.81 ± 0.19 | 4.86 ± 1.26 |
| | 200 | 13 | 2.08 ± 0.30* | 0.56 ± 0.11** | 3.19 ± 0.48* | 0.73 ± 0.20* | 4.57 ± 0.99* |

Relative heart weight was calculated by dividing the total heart weight (THW), left ventricular weight (LVW) and right ventricular weight (RVW) by body weight (BW). Relative lung weight was calculated in the same manner (lung weight/body weight, LW/BW). In addition, lung wet /dry weight ratio was also calculated. All data are expressed as mean ± s.d. *$P < 0.05$, **$P < 0.01$ vs vehicle control group.

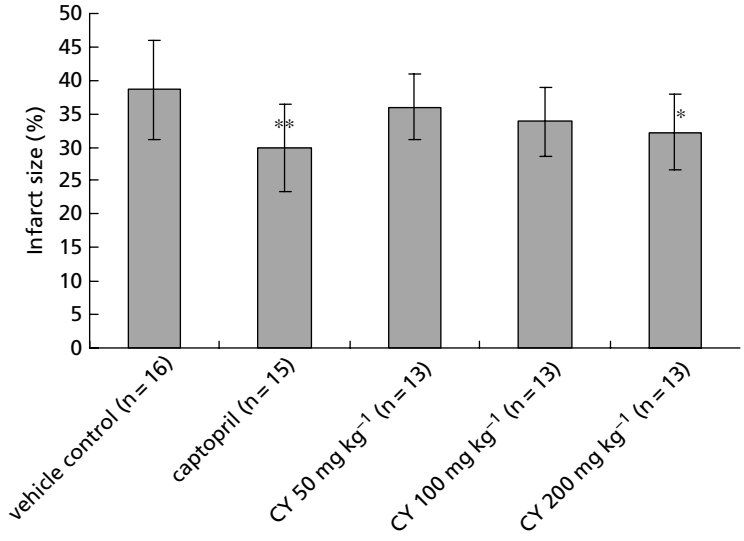


**Figure 2** Effect of *Corydalis yanhusuo* (CY) on infarct size (IS) in rats with heart failure. IS was determined as a percentage of left ventricle circumference. Each column represents the mean ± s.d. *$P < 0.05$, **$P < 0.01$ vs vehicle control group.

50 mg kg$^{-1}$, but not significantly (Figure 2). Infarct length (IL) was significantly reduced in *Corydalis yanhusuo* 200 and 100 mg kg$^{-1}$ groups (Table 3). As indexes for left ventricular dilation, the inner diameter of the left ventricle (LVD) and left ventricle circumference (LVC) were significantly reduced in *Corydalis yanhusuo* treatment groups in a dose-dependent manner (Table 3).

## Discussion

Myocardial infarction is one of the major causes of heart failure. Accordingly, rats that develop heart failure after induced left ventricular MI are widely used as experimental models of human congestive heart failure. The progression of disease in these rats

**Table 3** Effect of *Corydalis yanhusuo* on morphologic parameters of the hearts in heart failure rats

| Group | Dose (mg kg$^{-1}$) | Rat No. | IL (cm) | LVC (cm) | LVD (cm) |
|---|---|---|---|---|---|
| Sham | — | 13 | — | 2.25 ± 0.27 | 0.56 ± 0.08 |
| Vehicle | — | 16 | 1.08 ± 0.22 | 2.85 ± 0.17 | 0.74 ± 0.07 |
| Captopril | 50 | 15 | 0.71 ± 0.17** | 2.44 ± 0.19** | 0.61 ± 0.10** |
| *Corydalis* | 50 | 13 | 0.96 ± 0.09 | 2.70 ± 0.19 | 0.70 ± 0.07 |
| | 100 | 13 | 0.87 ± 0.13* | 2.60 ± 0.12* | 0.67 ± 0.05* |
| | 200 | 13 | 0.81 ± 0.16** | 2.53 ± 0.18** | 0.65 ± 0.05** |

IL, ischaemic length; LVC, left ventricle circumference; LVD, inner diameter of the left ventricle. IL (cm) = (endocardial + epicardial infarct length) × 1/2; LVC (cm) = (endocardial + epicardial length of the left ventricle) × 1/2; LVD (cm) = endocardial circumference /$\pi$. All data are expressed as mean ± s.d. *$P < 0.05$, **$P < 0.01$ vs vehicle control group

includes impairment of left ventricular function, induction of ventricular remodelling and activation of neurohumoral factors, closely resembling characteristics observed in patients with ischaemic heart failure (Garcia Gonzalez & Dominguez 2006; Greenberg et al 2006; Leontiadis et al 2006; Rizik et al 2006). Nine weeks after MI, the rats featured pronounced heart failure in the vehicle control group. Heart failure is associated with increased LVEDP and impaired myocardial contractility (±dp/dtmax). Cardiac hypertrophy was present as demonstrated by an increase in relative heart weight accompanied by left ventricle dilatation. The rats also showed signs of congestion heart failure as raised relative lung weight and lung wet weight/dry weight ratio.

*Corydalis yanhusuo* W.T., a famous Chinese medicinal herb, belongs to the Papaveraceae family. In traditional Chinese medicine practice, it is an important remedy for painful conditions. A number of alkaloids have been isolated from the tuber of *Corydalis*, including dehydrocorydaline, corydaline, *dl*-tetrahydropalmatine, protopine, tetrahydrocoptisine, tetrahydrocolumbamine and corybulbine (Fu et al 1986a, b). These alkaloids exhibit a wide number of pharmacological actions, including analgesic (Jin 1987), anti-arrhythmic (Wang et al 1993) and anti-hypertensive effects (Chan et al 1999), as well as strong cardiovascular actions (Chueh et al 1995; Xu et al 1996; Zeng et al 2000a).

We treated heart failure rats with *Corydalis yanhusuo* from the second week after MI for a period of 8 weeks, and then demonstrated its benefits on left ventricular dysfunction, pulmonary congestion and left ventricular dilatation. In contrast to previous studies (Ling et al 2006; Xuan et al 1992), which mainly examined the acute effects for MI, our results demonstrated that chronic treatment with *Corydalis yanhusuo* could improve cardiac function and structure in a postinfarction rat model of heart failure. Treatment with *Corydalis yanhusuo* significantly inhibited the elevation in LVEDP, which is a cardiac preload parameter, improved myocardial contractility as shown by higher ±dp/dtmax and reduced the lung wet weight/dry weight ratio, a sign of pulmonary congestion. Plasma level of ANP, a marker of neurohormonal activation, was also lowered in *Corydalis yanhusuo* treating rats. Furthermore, our studies showed that administration with *Corydalis yanhusuo* caused a significant prevention of compensatory hypertrophy as evidence by lower ratio of heart weight/body weight, as well as inhibition of cardiac dilation, suggesting attenuation of cardiac remodelling.

Heart failure is a complex disease involving many factors, such as the sympathetic nervous system, renin–angiotensin system, reactive oxygen species, apoptosis, and so on. The pathologic background of heart failure also consists of myocyte hypertrophy, apoptosis and interstitial fibrosis in the remote non-infarcted area. The extract from *Corydalis yanhusuo* contained approximately 10 alkaloids, such as dehydrocorydaline, corydaline, *dl*-tetrahydropalmatine, protopine, tetrahydrocoptisine, tetrahydrocolumbamine and corybulbine, that might exert miscellaneous cardioprotective activity through different mechanisms.

Recent studies from patients and animal models of heart failure have demonstrated that cardiomyocyte apoptosis is observed during development of heart failure. The accumulated myocyte apoptosis correlated significantly to the degree of myocardial dysfunction in the animal model of heart failure (Takemura & Fujiwara 2004; Razavi et al 2005). We have previously demonstrated that *Corydalis yanhusuo* could protect cardiomyocytes from apoptosis through increasing bcl-2 expression in cardiac tissues (Ling et al 2006). Another study also showed similar anti-apoptotic activity of *Corydalis yanhusuo* in a rat cerebral ischaemia model (Yang et al 2000; Liu & Yang 2004). In addition, tetrahydropalmatine, one of the main active principles, has been demonstrated to be a potent calcium-channel blocker (Xu et al 1996), and decreased the $Ca^{2+}$ level in ventricular myocytes in a dose- and frequency-dependent manner (Chan et al 1999). L-THP could inhibit the $Ca^{2+}$ overload of cultured rat cardiomyocytes during hypoxia and reoxygenation (Zeng et al 2000b), and had a moderate inhibitory effect on L-$Ca^{2+}$ current (Huang et al 1999). Since inhibition of L-type $Ca^{2+}$ channels has been shown to protect cardiomyocytes from apoptosis, some of the beneficial effects of *Corydalis yanhusuo* in heart failure rats were mediated in part by calcium channels in the heart as well as in the extra-cardiac tissues such as the vasculature and lung. Inhibition of L-type $Ca^{2+}$ channels may represent one of the mechanisms by which *Corydalis yanhusuo* protects cardiomyocytes from apoptosis.

The important role of neurohormonal activation in the progression of heart failure and left ventricular dysfunction is well established. Neurohomonal activation after acute MI refers to increased activity of the sympathetic nervous system, ANP and arginine vasopressin, etc. (Nakamura et al 2004; Sun et al 2005; Garcia Gonzalez & Dominguez 2006; Qin et al 2006). Angiotensin-converting enzyme inhibitors and $\beta$-adrenoceptor antagonists have been shown to interfere

with postinfarction remodelling, resulting in improved prognosis of heart failure. It has been reported that some alkaloids of *Corydalis yanhusuo*, such as *l*-tetrahydropalmatine, could reduce heart tissue noradrenaline level and decrease peripheral vascular resistance, as adrenergic receptor antagonists (Xu et al 1987; Chueh et al 1995; Lin et al 1996; Wu & Jin 1997). The results of this study are partly supported by this explanation.

Despite considerable scientific data on the biochemical characteristics of heart failure, the precise molecular mechanisms responsible for heart failure still remain poorly understood. Several additional mechanisms have recently been identified that could also be important, including inflammatory cytokines, nitric oxide, oxidative stress, endothelin and peptide growth factors. Whether the improved cardiac function observed with *Corydalis yanhusuo* is due to these mechanisms remains elusive; these aspects need further investigation.

## Conclusion

A growing body of evidence suggests that *Corydalis yanhusuo* is an effective agent for treating cardiovascular diseases. In this study, we demonstrated an important action of *Corydalis yanhusuo* giving protection in heart failure, particularly during the later phase after myocardial infarction. Precise studies on the effect of *Corydalis yanhusuo* and other traditional Chinese medicines may be helpful for improving treatment of cardiovascular diseases.

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