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Effect of functional food raw material *Peucedanum praeruptorum* Dunn: a research update

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Abstract

Peucedanum praeruptorum Dunn is a natural plant with expectorant, antitussive, anti-asthmatic, anti-inflammatory, antispasmodic and sedative effects. It is used in traditional Chinese medicine. The key active substances extracted after separation are also used to process functional food. Recent advances in the development of *Peucedanum praeruptorum* Dunn industrially have increased the market demand. In particular, the study of the physiological activity of *P. praeruptorum* Dunn has always been a research hotspot; however, limited data exist currently. This study reviews the research developments associated with the physiological activities of *P. praeruptorum* Dunn in terms of cardiovascular, expectorant and antitussive, antitumor, and anti-inflammatory effects. The results serve as a standard of reference for further investigation into the pharmacologic role of *Peucedanum praeruptorum* Dunn.

Keywords: *Peucedanum praeruptorum* Dunn; HepG2 physiological activity; anti-inflammatory; antitussive; anti-asthmatic.

Practical Application: *Peucedanum praeruptorum* Dunn is a kind of natural plant. Some active substances contained in it have been used in the processing of health food, but there are few applications and studies on it. This study summarizes the research on its role, which provides some new ideas and reference materials for better application. *Peucedanum praeruptorum* Dunn is the dry root of *Peucedanum praeruptorum* Dunn and purple *Peucedanum praeruptorum* Dunn belonging to family Umbelliferae. It tastes bitter and pungent, and is slightly cold. It effectively clears pulmonary congestion, resolving phlegm, alleviating heat and detoxifying the system. Nearly 130 types of plants are included in the genus *Peucedanum*. Approximately 30 types are distributed in China, and 7 are fully utilized. Clinical research shows that *Peucedanum praeruptorum* Dunn exhibits strong therapeutic response to wind-heat cough and asthma, cardiovascular diseases and cancer. It is a natural plant with robust physiological activity. Scholars have investigated the physiological activity of *Peucedanum praeruptorum* Dunn, but most of the studies are sporadic. This study summarizes the recent advances in the study of the physiological activity of *P. praeruptorum* Dunn, so as to provide a reference for further investigation.

1 Cardiovascular effects

1.1 Role in arrhythmia and heart failure management

Cardiomyocytes of guinea pigs were treated with a dose of 5 μmol·L^{-1}. The antiarrhythmic effect is very rapid. Treatment with a praeruptorin A (Pd-Ia), the active component of *P. praeruptorum* Dunn A at a dose of 50 μmol·L^{-1} enhanced the antiarrhythmic effect. Treatment with *P. praeruptorum* Dunn A shortened the action potential durations APD30, APD50 and APD100 of guinea pig cardiomyocytes (Feng et al., 1998). Pd-Ia also significantly shortened action potential amplitude (APA) of guinea pig ventricular myocytes. Exposure to a dose of 5 μmol·L^{-1} resulted in an increase in action potential from normal (90.82 ± 3.07) mV to (87.2 ± 3.51) mV. When the dosage was increased to 50 μmol·L^{-1}, the shortening effect was significant (85.41 ± 3.44 mV) and dose-dependent. These results suggest that PD-IA has an anti-arrhythmic effect, and the mechanism may be mediated via Ca^{2+}. The internal circulation channel is blocked. PD-IA reduces the heart weight-to-body weight ratio and also decreases the activity of serum creatine kinase and other enzymes via mechanisms similar to inhibition of calcium influx (Lin et al., 2007). In addition, PD-IA promotes the expression of nestin, which is significantly enhanced in both myocardial ischemic and infarcted cells. Therefore, it is believed that nestin expression is related to the regeneration and repair of myocardial cells to a certain extent.

Functional foods are some industrial processed or natural foods (Figure 1). When regularly consumed at an effective level in a variety of diets, they not only provide basic nutrition to the human body, but also have a potential positive impact on human health (Granato et al., 2020). Now common functional foods include probiotics (Long et al., 2022), active factors from natural sources (Khan et al., 2021; Jiang et al., 2021), foods composed of clear compound nutrients (Califa-Estwick et al., 2021; ur Rehman et al., 2021), etc. As a new source of food from a research perspective, *P. praeruptorum* Dunn may play a role in

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Figure 1. *Peucedanum praeruptorum* Dunn form and its application in food industry.

myocarditis; however, the role of nestin in myocardial ischemia and myocardial infarction (mi) is not clear, and requires further exploration. *P. praeruptorum* Dunn is a functional food for preventing myocarditis.

Because the synthesis and secretion of APN can promote the hypertrophy effect of cardiac myocytes, and ET-1 can promote the synthesis and secretion of adiponectin (APN) (Tu et al., 2006a). The results show that the drug-containing serum of *P. praeruptorum* Dunn extract (PD-E) inhibits the synthesis of ET-1, which inhibits the synthesis and secretion of APN to eventually reduce the hypertrophy of cardiomyocytes. PD-E enhances the expression of Bcl-2 and Bax proteins and the ratio of Bcl-2/Bax protein expression, and inhibits the apoptosis of cardiomyocytes induced by ventricular pressure overload (Tu et al., 2006b). The PD-E reduced the oxygen consumption of myocardium, promoted cardiac output, and inhibited the effects of heart failure[6].

P. praeruptorum Dunn water aqueous (Pd-wa) protects against barium chloride and symptoms of arrhythmia (Chang et al., 1991). The protective effect of Pd-wa against barium chloride-induced arrhythmia was observed in rats. Prophylactic administration of PD-E (aqueous & alcoholic) significantly reduced the duration of arrhythmia in rats. The PD-E (aqueous and alcoholic) inhibited barium chloride-induced arrhythmia in rats. Pd-wa administration prevented arrhythmia in rats immediately resulting in therapeutic effect. The duration of arrhythmia decreased from 5.5 ± 0.71 min (control group) to 0.58 ± 1.00 min ($P < 0.05$), and the duration of anti-arrhythmic effect persisted for 8.50 ± 5.01 min.

Some studies investigated the effect of propyl present in *P. praeruptorum* Dunn on hypertrophic rats with renal hypertension (Zhou et al., 2006). Propyl, one of the active components of *P. praeruptorum* Dunn, increased the arterial outflow/heart wet weight (AO/HWW) and coronary outflow/heart wet weight (CO/HWW) by 31.3% and 25.1%, respectively, in rats with renal hypertension and left ventricular hypertrophy. Thus, praeruptorin C (Pra-C) can increase coronary flow and cardiac output. The left ventricular systolic pressure (LVSP) and -dp/dt$_{max}$ of rats were also increased by 16.0% and 36.5%, respectively. In conclusion, Pra-C improves the myocardial systolic and diastolic function of rats with left ventricular hypertension (LVH). Pra-C was also reported to reduce the levels of hydroxyproline in left ventricular muscle during LVH to improve the myocardial compliance of rats. *P. praeruptorum* Dunn has a protective effect against heart injury caused by ischemia-reperfusion (Jiang et al., 2004b). Studies have shown that Pra-C promoted the recovery of coronary blood flow (CBF) and coronary outflow (CO) adversely affected in the heart during ischemia-reperfusion, and significantly reduced the levels of CK and calcium ions in the mitochondria. These results suggest its protective role in ischemia-reperfusion injury of rat heart.

The mechanisms of *P. praeruptorum* Dunn against arrhythmia and heart failure can be summarized as follows. Various components of *P. praeruptorum* Dunn affect cardiovascular function, via calcium antagonism, inhibition of myocardial hypertrophy, and improved myocardial systolic and diastolic function. Based on its physiological activities, *P. praeruptorum* Dunn is expected to be an effective functional food in cardiovascular intervention and prevention.

1.2 Protection against myocardial ischemia and myocardial infarction

Pretreatment with *P. praeruptorum* Dunn has a significant protective effect on myocardial cells of hypoxic reoxygenated rats. *P. praeruptorum* Dunn propyl reduced intracellular calcium concentrations and decreased apoptosis, thus demonstrating a

protective effect on injured rat cardiomyocytes by acting as a calcium antagonist (Chen & Zhu, 2007).

Studies have shown that *P. praeruptorum* Dunn and its active components modulate the expression of tumor necrosis factor-α and myocardial nuclear factor -κB induced by ischemia-reperfusion (Wang & Chang, 2003). Both *Peucedanum praeruptorum* Dunn and Pd-Ia inhibited the expression of NF-κB and TNF-α in I/R myocardium (Jiang et al., 2004a). Pd-Ia alleviated the reperfusion injury induced by myocardial ischemia in rats. The results showed that the activities of LDH, AST, CK and CK-MB in serum were affected by *P. praeruptorum* Dunn and the inhibition of myocardial ischemia-reperfusion injury in rats was stronger with *P. praeruptorum* Dunn extract. *P. praeruptorum* Dunn extract, prepared with 3.75g/mL of raw material, significantly increased the activity of superoxide dismutase in the serum of rats with reperfusion injury, suggesting the possible mechanism underlying the anti-myocardial ischemic effect. Treatment with *P. praeruptorum Dunn extract* administered via duodenum at a dose of 0.2/100 g/kg led to a decrease in the activities of serum LDH and CK-MB.

P. praeruptorum Dunn affected the levels of IL-6 and apoptosis proteins in myocardium after ischemia-reperfusion (Chang et al., 2003). *P. praeruptorum* Dunn ethanol extract significantly increased coronary flow in cats with acute myocardial infarction after a series of anaesthetic thoracotomy procedures. *P. praeruptorum* Dunn extract increased CSF and reduced +LVdp/ DT in anesthetized thoracotomy cats with 12 fingers, LVEDP, LVP, and CR, suggesting that EP can resist myocardial ischemia and reduce myocardial infarction following treatment with *P. praeruptorum* Dunn crude extract of root (0.5, 1.0, and 1.5g/kg) and *P. praeruptorum* Dunn methyl extract (0.5 mg/kg, 1.0 mg/kg, and 2.0 mg/kg). The results showed that treatment with both extracts reduced the levels of IL-6 in rats with myocardial ischemia-reperfusion injury, and also inhibited the expression of apoptosis-related genes Fas, Bax, and bcl-2 (Jiang et al., 2004b).

These results indicate that *P. praeruptorum* Dunn can reduce the size of myocardial infarction and protect against myocardial ischemia and apoptosis.

1.3 Vasodilation and anti-hypertensive effects

P. praeruptorum Dunn regulates the blood pressure of hypertensive rats and vascular resistance of dogs (Rao & Chen, 2001). It was found that the A, B, C and E components of *P. praeruptorum* Dunn dilate blood vessels with inducing drug resistance. The antihypertensive effect was mild and lasting. The higher the dosage of *P. praeruptorum* Dunn, the more obvious was the reduction in the resistance of vertebral and coronary arteries and lower was the limb vascular resistance. Studies have also shown that Pra-C improved K^+ in left ventricular hypertrophy by reversing the degree of hypertensive left ventricular hypertrophy$^+$, and the levels of Ca^{2+}-ATP, -ATPASE, and Na^+.

P. praeruptorum Dunn inhibited the plasma endothelin-1(ET-1) in patients with pulmonary hypertension (Wang et al., 2001a). *P. praeruptorum* Dunn extract (QF-8) inhibited the synthesis and release of ET-1 in venous plasma of patients with chronic obstructive pulmonary disease (COPD_ secondary to pulmonary hypertension, thereby lowering blood pressure.

P. praeruptorum Dunn exhibited pharmacologic effects in left ventricular hypertrophy and muscle cell hypertrophy of renal hypertensive rats (Rao et al., 2002). The results showed that coumarin, the main active component of *P. praeruptorum* Dunn, reduced the myocardial wet weight of the left ventricle and inhibited the hypertrophic effect of cardiac hypertrophy by reducing the resting calcium level in hypertrophic cardiomyocytes. The prophylactic intervention inhibited the intracellular calcium increase induced by KCl and increased the myocardial membrane and mitochondrial Na levels of cardiomyocytes$^+$. The effect of K^+-ATPASE activity and mitochondrial Ca^{2+}, Mg^{2+}, -ATPASE activity was better than reversal of non administration.

P. praeruptorum Dunn affects the pulmonary hemodynamics and blood flow margin in rats with pulmonary hypertension (Wang et al., 2001a). The increased blood viscosity of pulmonary circulation in rats with inflammatory pulmonary hypertension is attributed to multiple factors, such as RBC accumulation, platelet attachment and activation, inflammatory cell chemotaxis, and adhesion. The antagonism of the biological activity of PAF and inhibition of histamine release from mast cells inhibits the pulmonary vascular leakage and edema. The results also showed that *P. praeruptorum* Dunn could be used to prevent and control pulmonary hypertension by inhibiting the RBC cascade and the activation and aggregation of platelets.

P. praeruptorum Dunn plays a role in pulmonary hypertension induced by monocrotaline (Wang et al., 2000). The abnormal indices of pulmonary artery pressure, right heart index, pulmonary vascular injury, inflammatory cell infiltration, TNC expression and proliferation of vascular smooth muscle cells were reduced by oral administration of *P. praeruptorum* Dunn extract under concentration gradient. PPD inhibits the development of pulmonary hypertension and plays a significant role in hypoxic pulmonary hypertension in dogs (Wang et al., 2001b). The extract of *P. praeruptorum* Dunn (QF-3) significantly reduced the mean pulmonary dynamic pressure, diastolic pulmonary dynamic pressure, mixed blood oxygen partial pressure and blood oxygen transport in dogs with low acute hypoxic pulmonary hypertension. In addition, CO, CI and dRVP increased significantly. In conclusion, QF-3 can be used to prevent and treat pulmonary hypertension.

The role of *P. praeruptorum* Dunn in reversing pulmonary hypertension was studied (Kang et al., 1993). The reduction of systolic pressure and ventricular hypertrophy index in rats with hypoxic pulmonary hypertension was achieved using *P. praeruptorum* Dunn oral liquid (2.5g /100 g).

The petroleum ether extracts of *P. pratorum Dunn* can be used to relax norepinephrine-induced preconstriction of the pulmonary ring in humans and to reduce primary tension, with non-competitive antagonistic effects (Kang & Yu, 1994). Additional studies were conducted in order to reduce pulmonary vascular resistance and total pulmonary resistance in patients with obstructive or chronic pulmonary disease and secondary pulmonary hypertension using an oral decoction of 1g/mL *P. praeruptorum* Dunn (Xi et al., 1996).

Strong vasodilation and blood pressure-lowering effects associated with the use of this natural product suggest a potential role in prevention and treatment of hypertension, especially in the elderly and obese individuals..

2 Antitussive and expectorant effect

P. praeruptorum Dunn from Guangxi, China was extracted with water and ethyl acetate to concentrations of 5.0 g/kg and 10.0 g/kg, respectively, and administered to mice and guinea pigs intragastrically administration once a day for 7 days (Huang et al., 1995). The results showed that the extract of Guangxi *P. praeruptorum* Dunn prolonged the incubation period of cough in mice and guinea pigs, and decreased the frequency of cough, demonstrating significant antitussive effect.

The aqueous extract of *P. praeruptorum* Dunn was fed to mice, resulting in expectorant effect based on phenol red flushing test of respiratory tract (Wu et al., 2003). Other varieties of *P. praeruptorum* Dunn were effective in removing phlegm. The expectorant activity of white, fine and red *P. praeruptorum* Dunn was better than that of other *P. praeruptorum* Dunn varieties. The raw material was administered in a solution of 20 g/kg and administered intragastrically to rats via capillary tube method.

P. praeruptorum Dunn treatment after honey moxibustion also resulted in strong expectorant and antitussive effects in mice, release of phenol red (Zhang et al., 2010). The results showed that the output of phenol red increased significantly, and inhibited the cough induced by ammonia and prolonged the incubation period of cough in mice. Besides, it also prolonged the incubation period of asthma induced by histamine phosphate in guinea pigs. These effects were stronger than those of *P. praeruptorum* Dunn before moxibustion with honey.

The results showed that *P. praeruptorum* Dunn alleviated cough and removed phlegm. However, the studies are limited by the lack of analysis of different active ingredients contributing to the therapeutic effect. Analysis of key active ingredients, followed by isolation and identification, can elucidate the mechanism of expectorant and anti-tussant action of this natural product.

3 Anti-platelet aggregation

The active components of *P. praeruptorum* Dunn were extracted with ethanol and added to the platelet plasma of rabbit ear arteries treated with PAF (Zhang & Li, 2019). The results showed that the hydrophilic and ethyl acetate components, and the aqueous and alcoholic extracts of *P. praeruptorum* Dunn glycoside inhibited platelet aggregation induced by PAF, and the hydrophilic component was the best. PAF, in turn, generates AAI and BHR, which can cause asthma.

It can be concluded that *P. praeruptorum* Dunn glycoside is a potential active ingredient that inhibits platelet aggregation. It can be used in the prevention and management of asthma, and as a functional food. However, its mechanism of action has yet to be elucidated and evaluated in clinical trials.

4 Anti-tumor effect

The *P. praeruptorum* Dunn active ingredient elemene inhibits lymphatic metastasis in lymphomas by inhibiting the expression of P2X7R, and enhancing immunity and inhibiting tumor growth (Zhou et al., 2000). The high expression of Bcl-2 and the presence of HCA-F25/cI16A3 cell line both contribute to the development of liver cancer. However, elemene inhibits the expression of Bcl-2 and HCA-F25 /cI16A3 DNA precisely, resulting in anti-tumor effect. It was found that β -elemene inhibited the subcutaneous transplantation of Lewis lung cancer in mice, and the tumor inhibition rate was more than 30% (Fang et al., 2005). The side effects are substantially less compared with tegafur treatment. Therefore, β-elemene is effective for lung cancer prevention and management. The active compound β-elemene was injected intraperitoneally to prevent intracerebral glioma in mice, resulting in obvious analgesic and anti-tumor effects (Mao et al., 2001).

Thus, elemene exhibits significant anti-tumor effects with few side effects, specifically for the prevention of cancers of lung and liver. Therefore, the study of its mechanism is of great significance. Cancer seriously affects the quality of life, and routine intervention and prevention using the active ingredients of *P. praeruptorum* Dunn should be further investigated.

5 Anti-inflammatory effect

The effects of *P. praeruptorum* Dunn A on the activity of RAW264.7 cells cultured in vitro were analyzed via MTT assay (Li et al., 1994). The levels of iNOS, TNF-α, IL-1β, NO, NF-κB and IκB-α generated in RAW264.7 cells were analyzed. The herbal extract did not significantly affect the activity of RAW264.7, but significantly down-regulated the expression of NO and iNOS, TNF-α and IL-1β induced by LPS. The activation of NF-κB was inhibited by blocking the degradation of IκB-α, resulting in anti-inflammatory and anti-tumor effects. These results suggest that *P. praeruptorum* Dunn A may be a potential functional food for the prevention and management of atherosclerotic diseases. The mRNA expression of iNOS, TNF-α and IL-6 in LPS stimulated mouse macrophages was significantly increased. RAW264.7 cells were stimulated with *P. praeruptorum* Dunn at doses of 2, 4, 6, 8, and 16 μg/mL propyl, butyl, E and 1 μg/mL LPS, respectively (Wang et al., 2004). The extract significantly inhibited the release of inflammatory mediator NO in macrophages and the expression of iNOS, TNF-α and IL-6 mRNA in macrophages, suggesting that propyl, butyl and E exhibit anti-inflammatory effects.

6 Promotes blood circulation and removes blood stasis

PPD treatment decreases the whole blood viscosity at different shear rates, and significantly improves the pulmonary circulation of anesthetized rats (Hong et al., 2001). Another study showed that *P. praeruptorum* Dunn extract also had similar effects on increase in blood viscosity induced by hypoxia in dogs (Hong et al., 2000). PPD extracted from *P. praeruptorum* Dunn significantly improved erythrocytes in cases of pulmonary hypertension induced by monocrotaline (Wang et al., 2001a). Reducing the viscosity of pulmonary circulation at different shear rates effectively prevents pulmonary hypertension in rats.

7 Outlook

P. praeruptorum Dunn exhibits a wide range of physiological activities (Figure 2). Currently, however, most of the studies

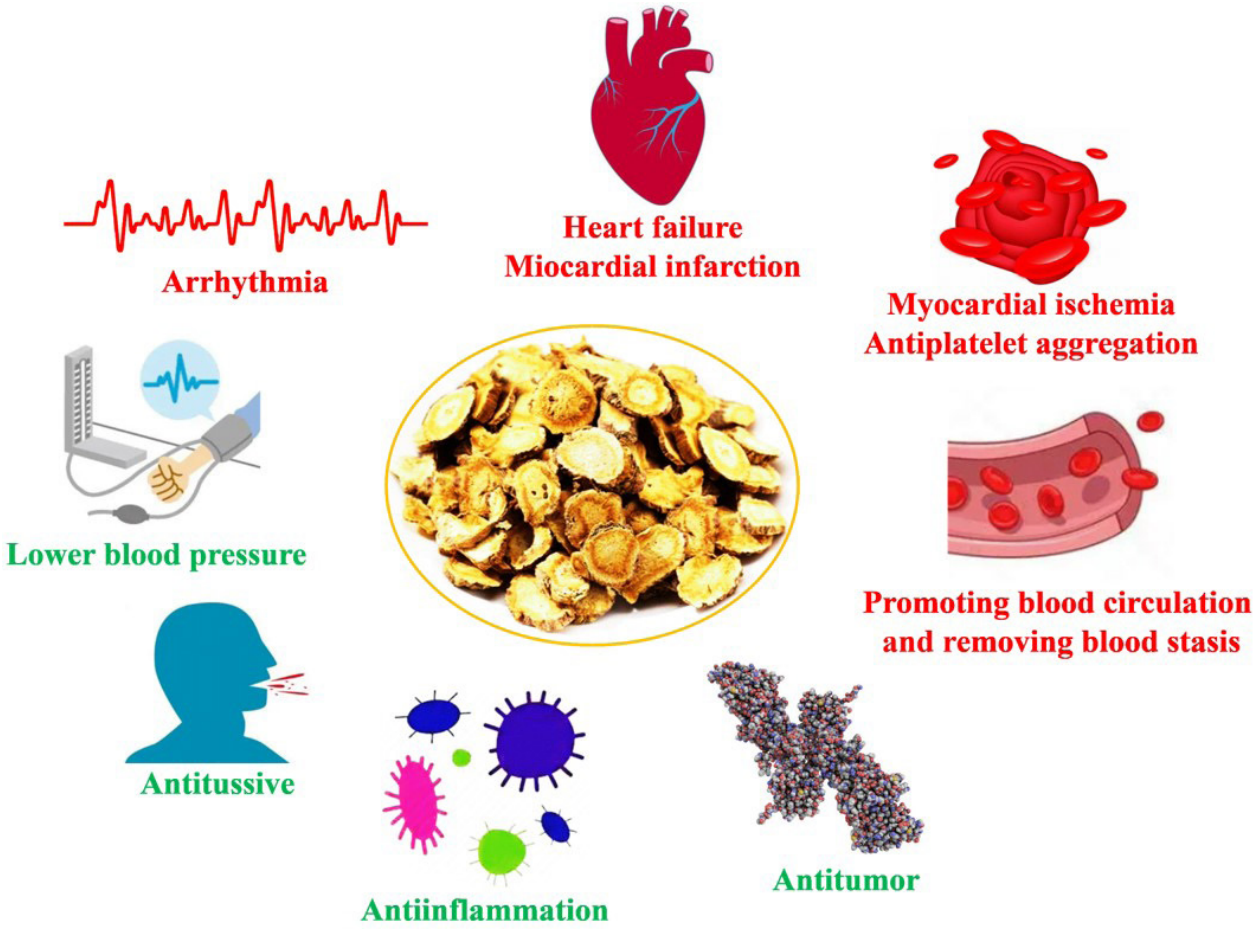

Figure 2. Biological activities of *Peucedanum praeruptorum* Dunn extract.

demonstrate significant cardiovascular effects and studies investigating other physiological effects are relatively rare. As a natural plant product, it is associated with few or even no side effects. Extraction and separation of active ingredients using modern biotechnology is of great value for the development of functional foods with clear functions and mechanisms.

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