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Keywords: Tashinones, SHR, Traditional herbs

Chronic essential hypertension is a major and the most common risk factor for developing cardiovascular disease. Despite the recent advancement in conventional drug therapy, compliance with antihypertensive drugs is still a common problem due to side effects. So it is still significant in the development of new antihypertensive drugs from natural products or traditional herbs.

Tashinones are purified from the dry root of *Salvia miltiorrhiza* Bge. (Labiatae), they are diterpene quinones isolated by Prof. Feng-Lin Hsu of the Graduate Institute of Pharmaconogsy of Taipei Medical University. In this study, we applied three doses, 20, 40 and 60 mg/kg of Tashinone on conscious spontaneous hypertensive rat (SHR). Thirty minutes after intraperitoneal injection of Tashinone, it decreased the blood pressure (BP) and the effects maintained for 90 minutes. Tashinone decreases the blood pressure in SHR in a dose-dependent manner. On the other hand, Tashinone didn't change the BPs of normotensive rats (WKY). These data suggested that Tashinone is an effective anti-hypertensive drug.

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Hypertension is one of the most important modifiable risk factors for coronary heart disease (the leading cause of death in the United States and many European nations), stroke (the third leading cause), congestive heart failure, end-stage renal disease, and peripheral vascular disease （1-4）. Improvements in the identification and treatment of hypertension have contributed to a major reduction in the incidence of cardiovascular disease in many countries（5,6）. Despite these advances in the detection and pharmacologic treatment of hypertension, inadequate blood pressure control continues to be a major public health problem（7）. Compliance with antihypertensive therapy may be an important barrier to optimal blood pressure control, as some antihypertensive drug treatments can have a negative impact on quality of life (QOL) （8,9）. Development of new antihypertensive agents that have good efficacy and tolerability and also could be regarded as natural products would be of considerable clinical interest, particularly in Oriental countries, where herbal preparations are viewed favorably by patients.

Injection of Tan Seng extract into the isolated heart of guinea pigs or rabbits (normal or atherosclerotic) caused relaxation of coronary vascular smooth muscle and an increase in coronary circulation. In anesthetized dogs, the intravenous injection of Tan Seng extract in a dose of 4 g/kg increased coronary flow by 70.5% and reduced resistance by 46% . Clinical trials with this extract in patients with coronary artery disease reported a definite increase in coronary circulation index (10).

The herb has a protective effect in acute myocardial ischemia. In experiments with animals in which myocardial ischemia was induced either by intracardial injection of norepinephrine (NE) or by partial ligation of a coronary branch, administration of *Tan Seng* extract reduced ischemic symptoms, improved the pathological electrocardiogram (ECG) pattern, and stimulated the regeneration of myocardial tissue. Tanshinone IIA, one of the active ingredients of the herb, and its water-soluble sulfonate salt were used clinically and showed an acceleration of coronary blood blow and collaterals by blocking Ca^{2+} entry（10）.

Tan Seng extract can dilate peripheral blood vessels, resulting in a drop in blood pressure. The effect can be blocked by atropine. Howevey, Tan Seng extract cannot reduce hypertension induced by norepinephine（10）.

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1. Animals

Male spontaneously hypertensive rats (SHRs, 350-450 g) and male Wistar-Kyoto rats (WKY) or Wistar rats (350-450 g) were used. They were obtained from the animal center of the National Cheng Kung University Medical College. Rats were housed in a temperature-controlled room (25±1℃) and kept on a 12hr : 12hr light-dark cycle (light on at 0600 h). Food (Purina Rat Chow) and water were available *ad labitum* throughout the experiment.

2. **Measurement of systemic blood pressure**

The systemic blood pressure was measured by a noninvasive tail-cuff monitor (UR-5000, Ueda Company, Japan) in conscious SHRs. The systolic blood pressure and heart rate of SHRs

can be recorded simultaneously. The SHRs (n=8), which had mean blood pressure higher than 160 mmHg were used to evaluate the antihypertensive activity of drugs. When the blood pressure was stable (varied less than 5 mmHg between 20 minute intervals), 20-60 mg kg^{-1} Tashinones (dissolved in normal saline) were administered intraperitoneally into SHRs. Other group of SHRs (n=8) received the same volume of normal saline as control. The systolic blood pressure was measured repeatedly 30,60,90 and 120 minutes after the injection of tashinones.

3. Statistics

All values were presented as mean ± standard error of mean. All experimental animal groups or experiments were 8 unless specified. ANOVA and Dunnetts post-hoc test was used to evaluate data between different experimental groups. A p value less than 0.05 was regarded as significant.

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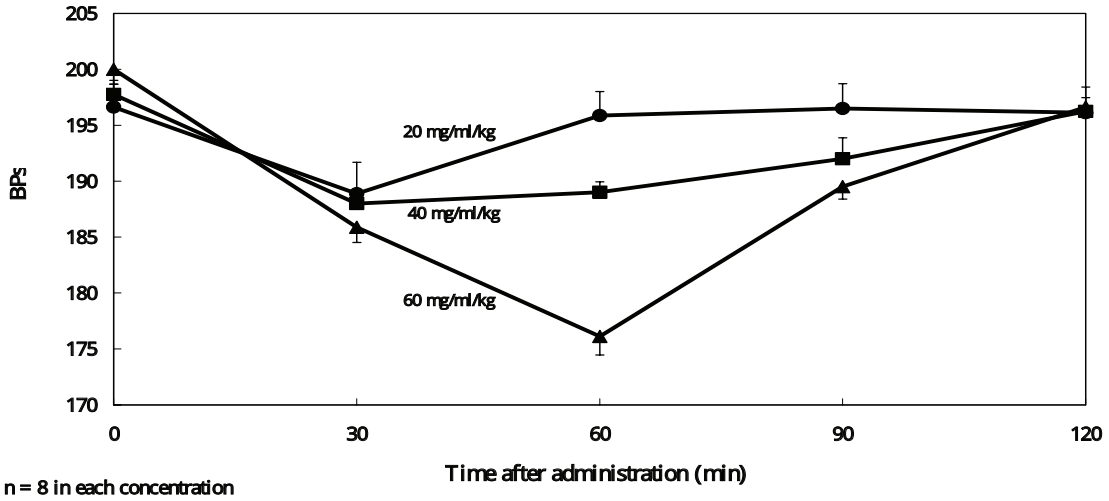
Antihypertensive activity of Tashinone IIA into SHR



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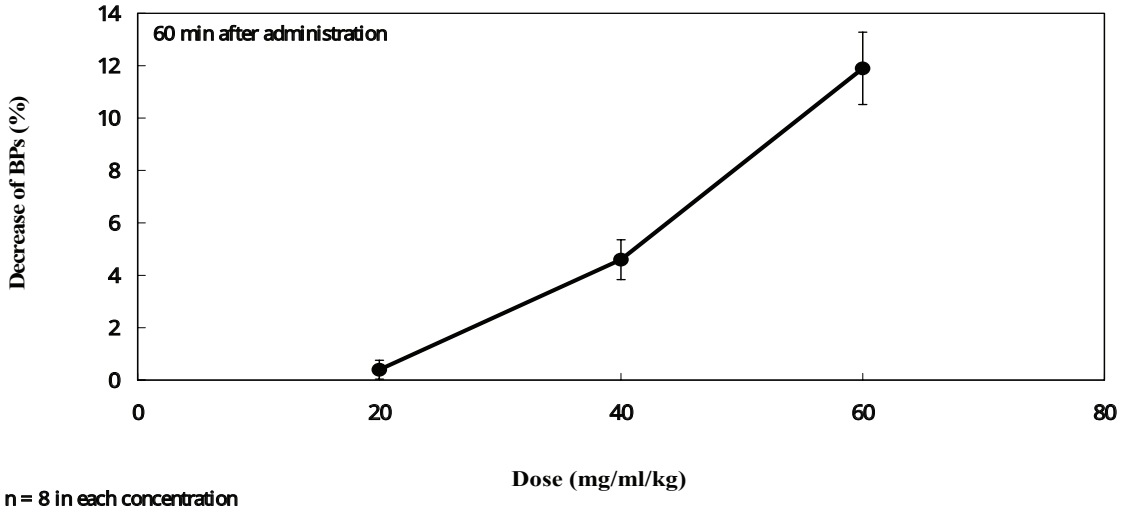
Decrease of blood pressure by Tashinone IIA into SHR



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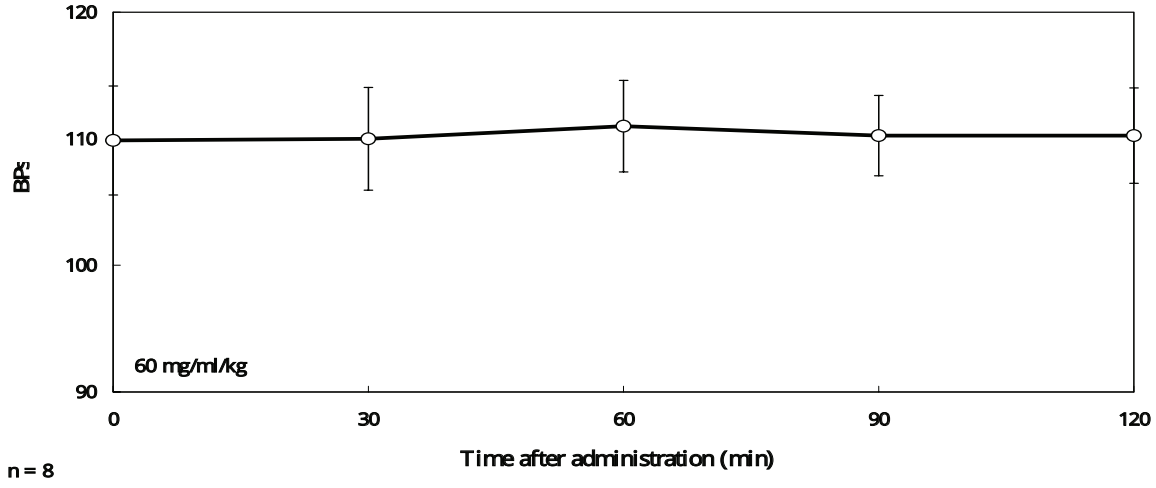
Antihypertensive activity of Tashinome IIA into WKY



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