Supporting Information

The Anaphylactoid Constituents in Xue-Sai-Tong Injection

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**Anaphylactoid activity assay of Xue-Sai-Tong injection in vivo**

Twenty-four healthy male guinea pigs, weighing 250-350 g were randomly divided into 4 groups (n = 6). Xue-Sai-Tong injections of 1.6 mL (equivalent dose of eight times injected to human) were injected into the marginal ear vein. Compound 48/80 (3.0 mg/mL) and normal saline solutions of 1.6 mL were injected as the positive and negative control group, respectively. Pathological changes were observed in lung tissue sections. Structure variation of pulmonary alveoli and inflammatory cell infiltration could be observed in the experimental groups of lung tissue sections. The result showed that Xue-Sai-Tong injection has potential anaphylactoid activity in vivo and histamine could be an index to evaluate the anaphylactoid ability of an herbal medicine injection.

![Fig. 1S Pathological changes of lung tissue caused by Xue-Sai-Tong injection (10 × 20)](image)

- a: control; b: compound 48/80; c: 20091108, normal hemolysis; d: 20091006,
abnormal hemolysis.

“→” : Pathological changes of pulmonary alveoli.

**Determination of ginsenoside-Rd-BSA conjugate by matrix-assisted laser desorption tof mass spectrometry**

Ginsenoside-Rd-BSA conjugate was synthesized as follows: 0.7 mL of methanol solution (80%, v/v) containing ginsenoside-Rd (10 mg) was added to a water solution (0.5 mL) containing NaIO₄ (4 mg). The solution was stirred at room temperature for 2 h. Carbonate buffer solution (50 mM, pH 9.6, 1.0 mL) containing BSA (10 mg) was added to the above reaction solution and the mixture was stirred at room temperature for another 5 h. Then, the mixture solution was centrifuged with an ultrafiltration device (3 KDa) at 8000 r/min for 1 h, and then lyophilized to produce ginsenoside-Rd-BSA conjugate (13 mg).

The mixture was placed inside a MALDI TOF/TOF 4800 plus mass spectrum (ABI Sciex) and irradiated with an N₂ laser (337 nm, 3 ns pulse). The ions formed by each pulse were accelerated by a 20-kV. Matrix solutions containing trifluoroacetic acid (0.1%, v/v) were prepared with acetonitrile and absolute methanol at the ratio of 7:3. 0.6 μL of the equivalent volume mixture of sample solutions with different concentrations (16 pmol/μL, 8 pmol/μL, 4 pmol/μL, 2 pmol/μL) and matrix solution were dropped on the sample target, dried at the room temperature, and measured at the linear model. The data was conducted by 4000 Series Explorer Software.

The MALDI tof mass spectrum of ginsenoside-BSA conjugate is shown in **Fig. 2S**. It showed the mass spectra of the conjugate of ginsenoside-Rd and BSA. A sharp peak coinciding with the conjugate appeared at \( m/z \) 74181.7832 (average for quadruplicates, c.v.: 0.37%), using a molecular weight of 66267 Da for BSA. According to previous research, the calculated value of the ginsenoside-Rd (947) residue is 7254 resulting in 8 molecules of ginsenoside-Rd conjugated with BSA.
Fig. 2S. MALDI mass spectrometry of the G-Rd-BSA conjugate