中药组方“虎诃紫”的急性毒性试验及对鸡白痢的临床疗效
代如意1, 殷中琼1, 贾仁勇1,2, 李莉1, 李曼1, 康帅1, 彭练意1, 曲径1
(1 四川农业大学 动物医学院, 四川 雅安 625014; 2 四川农业大学 预防兽医研究所, 四川 江苏 611130)
摘要: [目的]探讨中药组方“虎诃紫”的毒性及对鸡白痢沙门菌 Salmonella pullorum 的疗效。[方法] 根据药理研究技术指导原则, 对中药组方提取物进行小鼠灌胃急性毒性试验, 同时以人工诱发鸡白痢沙门菌的雉鸡感染模型, 按高、中、低(4.20, 1.62, 0.48 g/d) 剂量饮水给药, 临床 7 d, 评价中药组方“虎诃紫”颗粒剂的疗效。[结果和结论] 急性毒性试验给药剂量大于 5 000 mg/kg, 小鼠无死亡, 即 LD50 > 5 000 mg/kg, 对其进行中药组方提取物最大耐受量的测定, 其最大耐受量为 40 g/kg; 高剂量颗粒剂治愈率和有效率分别为 75.0% 和 83.3%, 中剂量颗粒剂的治愈率和有效率分别为 62.5% 和 75.0%, 而感染对照组的死亡率为 40%; χ2 检验表明“虎诃紫”颗粒剂, 中剂量组与感染对照组的死亡率差异显著 (P < 0.05)。结果表明: 中药组方无毒; 高剂量组的治愈率, 有效率都高于中, 低剂量组, 高, 中剂量组的死亡率都低于感染对照组, 说明高, 中剂量组对鸡白痢沙门菌的死亡具有一定的保护作用。
关键词: 中药组方“虎诃紫”; 急性毒性试验; 鸡白痢沙门菌; 疗效

An acute toxicity test of compound traditional Chinese medicine “Huhezi” and its efficacy in chickens experimentally infected with Salmonella pullorum
DAI Ruyi1, YIN Zhongqiong1, JIA Renyong1,2, LI Li1, LI Man1, KANG Shuai1, PENG Lianci1, QU Jing1
(1 College of Veterinary Medicine, Sichuan Agricultural University, Ya’an 625014, China;
2 Preventive Veterinary Research Institute, Sichuan Agricultural University, Wenjiang 611130, China)
Abstract: [Objective] To investigate the toxicity of compound traditional Chinese medicine “Huhezi” and observe its efficacy in chickens experimentally infected with Salmonella pullorum. [Methods] According to the veterinary drug research technical guidelines, the acute toxicity test was carried out in mice by gavage with “Huhezi” extracts. To evaluate the efficacy of “Huhezi” granules, the chickens experimentally infected with Salmonella pullorum were treated at a dosage of 4.20, 1.62, 0.48 g/d respectively by drinking water for 7 successive days. [Result and conclusion] The dose of acute toxicity test of “Huhezi” extracts was over 5 000 mg/kg. No death was observed in mice, revealing LD50 > 5 000 mg/kg. The maximum tolerated dose was 40 g/kg. The cure rates of different dose granules groups were 75.0%, 72.7%, 62.5% and the effective rates were 83.3%, 81.8%, 75.0% respectively, while the mortality rate of infected control group was 40%. The result of χ2 test showed that the mortality rate of high and medium dose group of “Huhezi” granule was significantly different from that of the infected control group. The results indicate that compound traditional Chinese medicine extracts are non-toxic, and the high and medium dose of “Huhezi” granules have certain protection to infected death of S. pullorum, with cure rates...
and effective rates of high dose group being higher than that of medium and low dose groups, the mortality rates of high and medium dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.

**Key words:** compound traditional Chinese medicine “Huhezi”; acute toxicity test; *Salmonella pullorum*; curative effect

Chicken coccidiosis *Salmonella pullorum* affects various species, with rates of 2-3 weeks old and higher, reaching in the chicken up to 90% and in the broiler up to 50%, causing serious economic losses. The disease is caused by bacteria in the *Salmonella* genus, and the main pathogen is *Salmonella pullorum*. The disease affects young chickens, the mortality rates of the medium and low dose groups being lower than that of the infected control groups.
2 结果与分析

2.1 中药组方提取物的急性毒性试验

预试验中药组方提取物剂量为 10～40 g/kg，小鼠灌胃后出现暂时不适，未见中毒症状或死亡，说明 LD₅₀ 大于 5 000 g/kg 是实际无毒药物，只需测定最大耐受量，按照等比间距末测定出中药组方提取物的最大耐受量。当灌胃小鼠剂量达到 50 g/kg，小鼠出现精神萎靡，行动迟缓，食欲不振，12 h 后 10 只小鼠全部死亡，其他组表现中毒症状同上，但随着中毒剂量逐渐降低，24 h 内存活者基本正常，中药组方提取物灌胃剂量大于 40 g/kg 有小鼠死亡，即中药组方提取物的最大耐受量为 40 g/kg（表 2）。

| 表 2 中药组方提取物对小鼠的最大耐受量
| Chinese herbal compound extract maximum tolerated dose in mice results
<table>
<thead>
<tr>
<th>阵次/(g·kg⁻¹)</th>
<th>小鼠数/只</th>
<th>死亡数/只</th>
<th>死亡率/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5</td>
<td>10</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>25.0</td>
<td>10</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>37.5</td>
<td>10</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>50.0</td>
<td>10</td>
<td>10</td>
<td>100</td>
</tr>
</tbody>
</table>

2.2 “虎河紫”颗粒剂对鸡白痢沙门菌治疗效果

对治疗人工感染的鸡白痢沙门菌病使用的“虎河紫”颗粒剂的剂量不同，其治疗效果也有所差异，详见表 3。“虎河紫”颗粒剂的高剂量组的治愈率和相对增重量率分别大于中、低剂量组，其死亡率低于中、低剂量组，中剂量组治愈率和相对增重量率分别大于低剂量组，其死亡率低于低剂量组。“虎河紫”颗粒剂相对增重量率高，中、低剂量组，庆大霉素组与感染对照组的死亡率差异显著（P < 0.05），“虎河紫”颗粒剂高，中，低剂量组与庆大霉素组治愈率，有效率差异不显著（P > 0.05）。

| 表 3 “虎河紫”颗粒剂对鸡白痢沙门菌的临床试验结果
| Results of clinical trials of “Huhezi” granules on Salmonella pullorum
<table>
<thead>
<tr>
<th>组别</th>
<th>动物数/只</th>
<th>死亡率/%</th>
<th>治愈率/%</th>
<th>有效率/%</th>
<th>相对增重量率/%</th>
<th>与感染组相比(死亡率)</th>
<th>与庆大霉素组相比(治愈率)</th>
</tr>
</thead>
<tbody>
<tr>
<td>“虎河紫”颗粒剂高剂量组</td>
<td>15</td>
<td>23</td>
<td>75.0</td>
<td>83.3</td>
<td>92.94</td>
<td>45.93</td>
<td>2.82</td>
</tr>
<tr>
<td>“虎河紫”颗粒剂中剂量组</td>
<td>15</td>
<td>25</td>
<td>72.7</td>
<td>81.8</td>
<td>90.90</td>
<td>43.24</td>
<td>2.53</td>
</tr>
<tr>
<td>“虎河紫”颗粒剂低剂量组</td>
<td>15</td>
<td>36</td>
<td>62.5</td>
<td>75.0</td>
<td>89.30</td>
<td>33.86</td>
<td>1.62</td>
</tr>
<tr>
<td>庆大霉素组</td>
<td>15</td>
<td>13.3</td>
<td>86.7</td>
<td>88.9</td>
<td>85.98</td>
<td>58.84</td>
<td></td>
</tr>
<tr>
<td>感染对照组</td>
<td>15</td>
<td>40</td>
<td>87.2</td>
<td>78.27</td>
<td>66.67</td>
<td>40.60</td>
<td></td>
</tr>
<tr>
<td>健康对照组</td>
<td>15</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1) χ²₀.₀₅,₁ = 3.84, χ²₀.₀₁,₁ = 6.63.
3 讨论

中药组方“虎诃紫”是通过大量筛选中药得到治疗鸡白痢沙门菌的新药组方，为确保新药本身无毒性更能有效地治疗鸡白痢沙门菌，本试验通过急性试验来验证新药组方的安全性。急性毒性是评价兽药常用的方法之一，急性毒性试验是药物毒理学安全性评价的第一步，具有了解兽药急性毒性作用的重要作用。本研究结果表明，中药组方提取物量分别为10, 20, 30, 40 g/kg 时对大小鼠进行灌胃，大小鼠全部存活，根据毒性等级评价[11,13]，当 LD₅₀ > 5 000 mg/kg 时为实际无毒，而本组提取物在40 g/kg 时大小鼠都未有死亡，其 LD₅₀ 远远高于5 000 mg/kg，说明该中药组方为实际无毒组方，安全可靠。

中药组方“虎诃紫”颗粒剂由虎杖、诃子和紫花地丁3 种中药共同组成，颗粒剂作用具有清热解毒，涩肠止泻，敛肺生津，降火利痰，肺虚喘咳，久嗽不止，凉血消肿等[11]，同时虎杖、诃子和紫花地丁都有抗菌作用[12-14]，而本研究中也表明这3 味中药组成的组方对人工感染引起的鸡白痢沙门菌具有良好的治疗效果，治疗效果随着剂量的增加而更好。中高、中剂量组的有效率与阳性对照庆大霉素组相差不大，而治愈率稍高于庆大霉素，总体而言治疗效果与庆大霉素差异不显著。但高、中剂量组的相对增长率均高于庆大霉素组和感染组，这可能与中药含有多种营养物质和生物活性物质，在治病的同时能调节生理机能有关。

有报道以石榴皮、地榆、诃子等药物为主药组成“白润康”制剂，发现其对鸡白痢沙门菌人工感染鸡进行预防和治疗，保护率达 88% ~ 90%，治愈率 75.0% ~ 84.4%[15]。与本研究“虎诃紫”颗粒剂高剂量组 83.3% 的有效率和 75.0% 的治愈率相似。胡庭俊等[8]报道的马尾藻多糖纳米脂质体对鸡白痢沙门菌高剂量组的死亡率与本试验的死亡率也相符，表明“虎诃紫”对鸡白痢沙门菌治疗效果良好。

中药资源丰富，价格相对较低，兼具营养和治病双重作用，无残留，不易产生耐药性等，而“虎诃紫”颗粒剂安全无毒，对人工感染鸡白痢沙门菌具有良好的治疗效果和明显的质量增加作用，具有较好的临床推广意义。

参考文献：


【责任编辑 梁 瑛】

http://xuebao.scau.edu.cn