Adjuvant potential of angiotensin-(1-7) in attenuating organ dysfunction in septic rats with peritonitis

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Background and Goal of Study:
Sepsis is a systemic inflammatory reaction that may lead to multiple organ damage, shock and death. The renin-angiotensin system consists of two opposing axes; the ´classical axis´ mediated primarily by angiotensin II (Ang II), and the ´alternative axis´ mediated mainly by angiotensin-(1-7) (Ang-(1-7)).
Ang-(1-7) is a counter regulatory mediator of Ang II, which also appears to be protective against cardiovascular disease. In addition, Ang-(1-7) has been proposed to improve acute lung injury and fibrosis induced by endotoxin. However, its effect on multiple organ injury induced by sepsis remains unclear. Therefore, this study was to evaluate the Ang-(1-7) effect on the development of multiple organ dysfunction in septic rats and to explore the possible mechanism.

Materials and Methods:
Cecal ligation and puncture (CLP) was performed to induce a polymicrobial sepsis peritonitis model in male Wistar rats. Subsequently, the animals were randomly assigned to receive an intravenous infusion of Ang-(1-7) (1 mg/kg for 1 h) or an equivalent volume of vehicle (0.9% saline) solution at 3 and 6 h after surgical procedure. All hemodynamic and biochemical parameters were measured during the 24h observation.

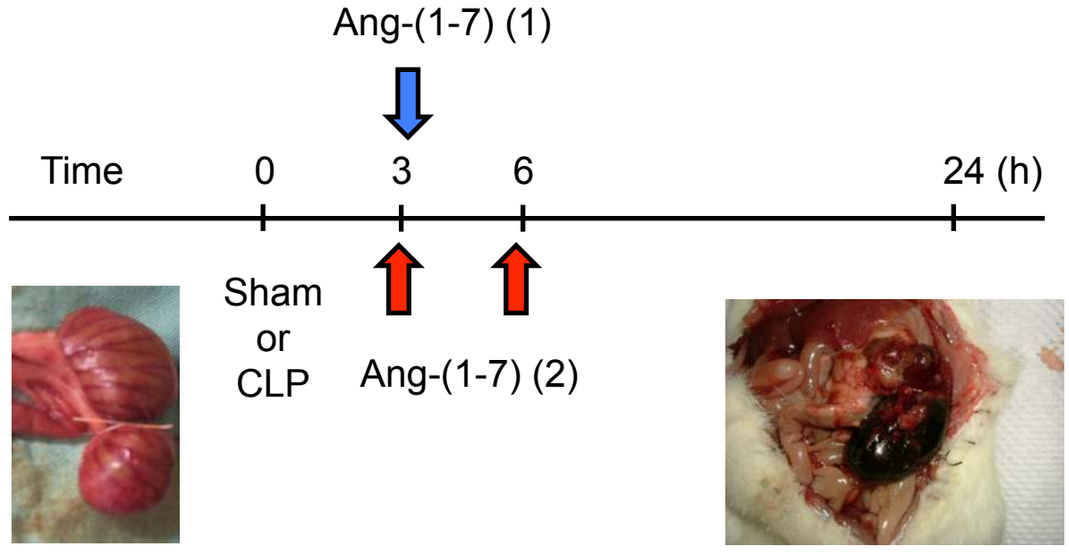

Figure 1. Effects of Ang-(1-7) on mean arterial pressure and heart rate

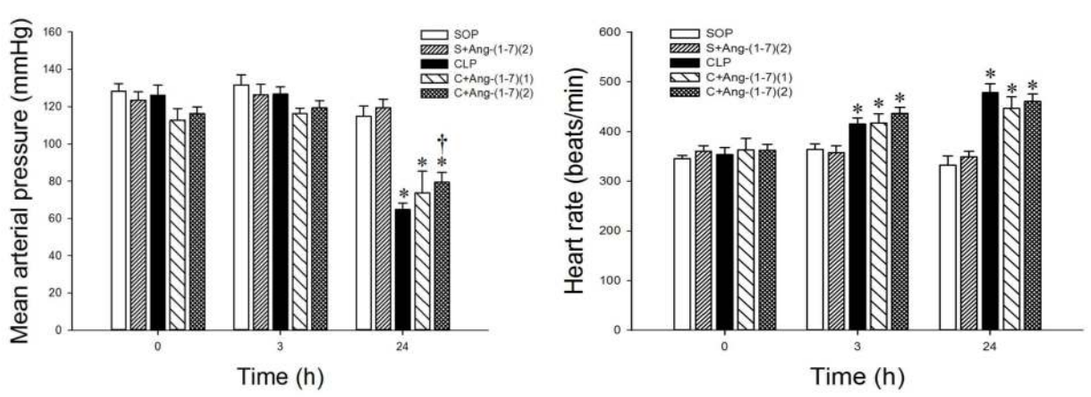

Figure 2. Effects of Ang-(1-7) on blood sugar and serum LDH

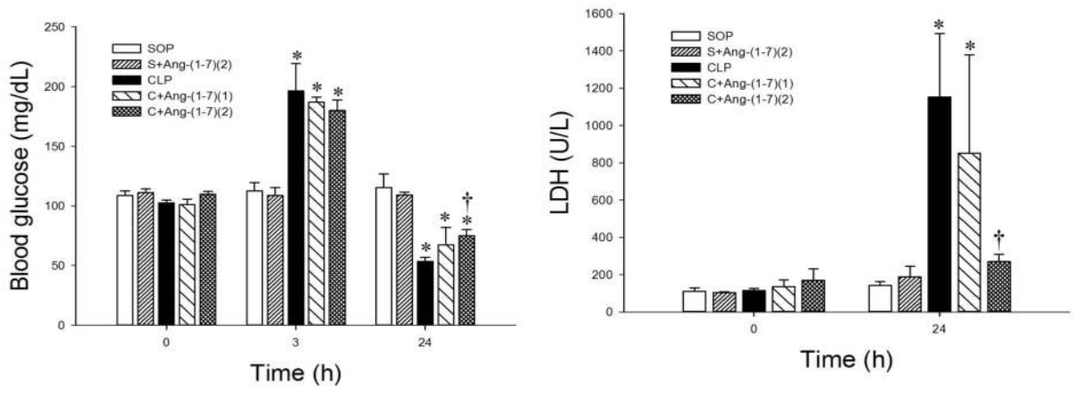

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Figure 3. Effects of Ang-(1-7) on serum BUN and creatinine

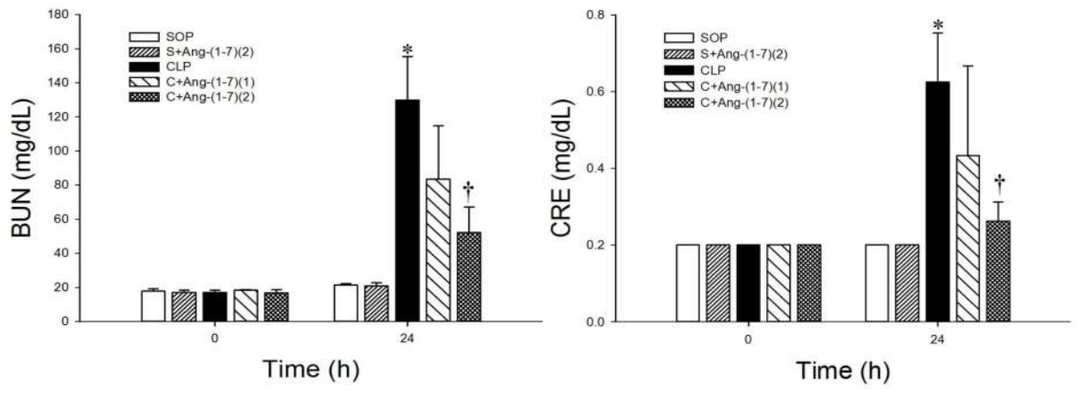


Figure 4. Effects of Ang-(1-7) on serum ALT and IL-6

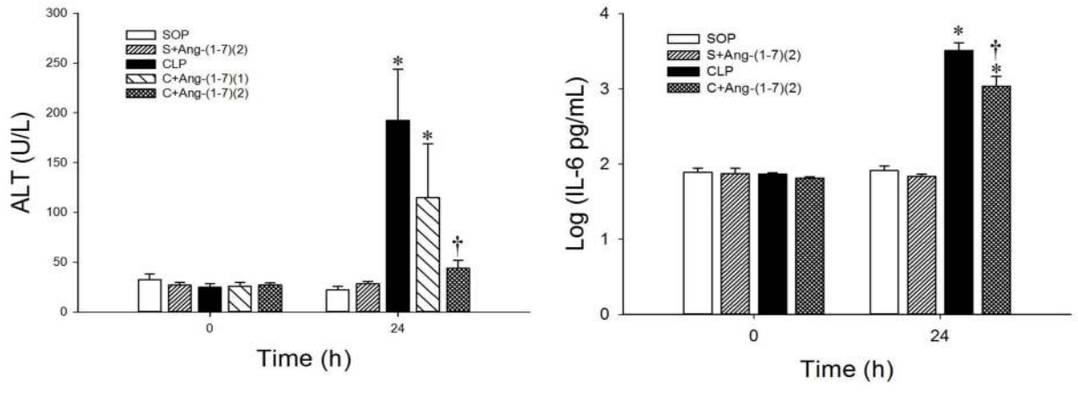


Figure 5. Effects of Ang-(1-7) on tissue superoxide and liver caspase-3

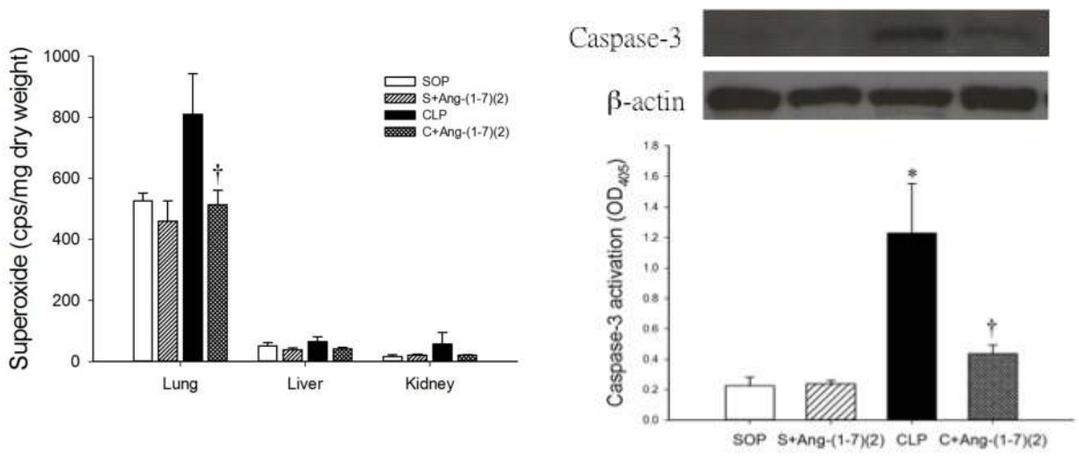
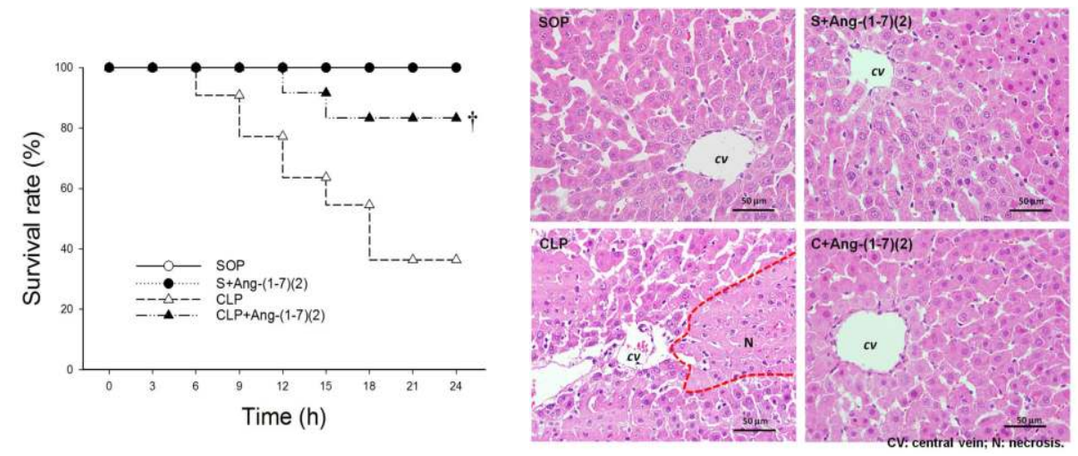


Figure 6. Effects of Ang(1-7) on survival and liver pathology



Conclusion:
Ang-(1-7) prevented circulatory failure, alleviated multiple organ dysfunction, and decreased the mortality rate in septic rats receiving CLP. These beneficial effects of Ang-(1-7) may be attributed to reducing tissue superoxide levels. Therefore, Ang-(1-7) could be a potential therapeutic adjuvant in the early sepsis.