



## Daphnetin Protected Against Lipopolysaccharide-induced Disseminated Intravascular Coagulation by Inhibiting Inflammatory and Coagulation Activation

Guopeng PAN<sup>2</sup> #, Yuanying LAI<sup>2</sup> #, Lin ZHI<sup>2</sup>, Fang WANG<sup>2</sup>,  
Lifei ZHU<sup>1</sup>, Kanglong MA<sup>2</sup> & Liang-Cai WU<sup>1</sup> \*

<sup>1</sup> *The 6th Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China*

<sup>2</sup> *Department of Pharmacology, Medical College, Jinan University, Guangzhou, Guangdong, China*

**SUMMARY.** Daphnetin is a bioactive ingredient extracted from *Daphne odora*, which has anticoagulant and anti-inflammatory effects. Disseminated intravascular coagulation (DIC) has clinical symptoms of hemorrhage, organ damage, and hemolysis. This study was designed to evaluate the therapeutic effects of daphnetin in LPS-induced DIC and to explore its mechanism. DIC model in BALB/c mice were established through intraperitoneal infusion of 60 mg/kg lipopolysaccharide (LPS). Similarly, in the treatment groups, 25, 50, and 100 mg/kg daphnetin were given. The efficacy of daphnetin on LPS-induced DIC was evaluated by measured coagulation parameters, organ damage and the levels of inflammatory cytokines. Daphnetin repaired coagulation disorders and reduced the damage of kidney and liver caused by LPS-induced DIC. In addition, daphnetin significantly decreased the production of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6). *In vitro* RAW 264.7 macrophage cells inflammatory model, daphnetin could inhibit nuclear factor-kappa B (NF- $\kappa$ B) signaling pathway. This study showed that daphnetin had excellent anticoagulant and anti-inflammatory effects and could be used as a potential drug for the treatment of DIC.

**RESUMEN.** La daphnetina es un ingrediente bioactivo extraído de *Daphne odora*, que tiene efectos anticoagulantes y antiinflamatorios. La coagulación intravascular diseminada (DIC) tiene síntomas clínicos de hemorragia, daño a los órganos y hemólisis. Este estudio fue diseñado para evaluar los efectos terapéuticos de la daphnetina en DIC inducida por LPS y para explorar su mecanismo. El modelo DIC en ratones BALB/c se estableció mediante infusión intraperitoneal de 60 mg/kg de lipopolisacárido (LPS). De manera similar, en los grupos de tratamiento se administraron 25, 50 y 100 mg/kg de daphnetina. La eficacia de la daphnetina en la DIC inducida por LPS se evaluó mediante los parámetros de coagulación medidos, el daño a los órganos y los niveles de citoquinas inflamatorias. La daphnetina reparó los trastornos de la coagulación y redujo el daño del riñón y el hígado causado por la DIC inducida por LPS. Además, la daphnetina redujo significativamente la producción de factor de necrosis tumoral alfa (TNF- $\alpha$ ) e interleucina-6 (IL-6). En el modelo inflamatorio de células de macrófagos RAW 264.7 *in vitro*, la daphnetina podría inhibir la vía de señalización del factor nuclear kappa B (NF- $\kappa$ B). Este estudio demostró que la daphnetina tenía excelentes efectos anticoagulantes y antiinflamatorios y podría utilizarse como un fármaco potencial para el tratamiento de la CID.

**KEY WORDS:** daphnetin, disseminated intravascular coagulation, lipopolysaccharide, NF- $\kappa$ B.

\* Author to whom correspondence should be addressed. *E-mail:* 1026871634@qq.com

# These authors should be considered as co-authors; they contributed equally to this study