

## Edgeworin Ameliorates Oxidative Stress and Accumulation of ECM Induced by High Glucose in Mesangial cells via Nrf2/TGF- $\beta_1$ Pathway

Yafeng LI <sup>1</sup> #, Yuanxia CUI <sup>1</sup> #, Huankai YAO <sup>2</sup>, Yan LI <sup>2</sup>, Shuo DING <sup>1</sup> \* & Yonggang CHEN <sup>3</sup> \*

<sup>1</sup> Fengxian People's Hospital, Xuzhou,  
Jiangsu 221700, China

<sup>2</sup> School of Pharmacy & Jiangsu Key Laboratory of New Drug Research and Clinical Pharmacy,  
Xuzhou Medical University, Xuzhou, Jiangsu 221004, China

<sup>3</sup> Department of Clinical Pharmacy, Xuzhou Central Hospital,  
Xuzhou, Jiangsu 221009, China

**SUMMARY.** Diabetic nephropathy (DN) is one of the severe complications of diabetes mellitus and become the major cause of end-stage renal disease. In the discovery of novel therapy targeting DN, phytochemicals play a pivotal role. Edgeworin is a natural dicoumarin with the potential to attenuate DN. To reveal the effects and detailed mechanisms, we have explored edgeworin using human mesangial cells under high glucose. The results showed edgeworin protected mesangial cells against oxidative stress and accumulation of extracellular matrix induced by high glucose. Further investigations unraveled the protection was closely associated with Nrf2, which is activated in a Keap1-dependent manner. These results can provide evidences for the application of edgeworin in clinic and discovery of novel therapy for DN.

**RESUMEN.** La nefropatía diabética (DN) es una de las complicaciones graves de la diabetes mellitus y se convierte en la principal causa de enfermedad renal terminal. En el descubrimiento de nuevas terapias dirigidas a la DN, los fitoquímicos desempeñan un papel fundamental. Edgeworin es una dicumarina natural con el potencial de atenuar la DN. Para revelar los efectos y los mecanismos detallados, hemos explorado la edgeworin utilizando células mesangiales humanas en condiciones altas de glucosa. Los resultados mostraron que la edgeworin protegía las células mesangiales contra el estrés oxidativo y la acumulación de matriz extracelular inducida por niveles elevados de glucosa. Investigaciones adicionales revelaron que la protección estaba estrechamente asociada con Nrf2, que se activa de manera dependiente de Keap1. Estos resultados pueden proporcionar evidencia de la aplicación de edgeworin en la clínica y el descubrimiento de una nueva terapia para la ND.

**KEY WORDS:** diabetic nephropathy, edgeworin, extracellular matrix, mesangial cells, Nrf2, oxidative stress.

# These authors contribute equally to this work.

\* Authors to whom correspondence should be addressed. *E-mails:* jsfxrmyyds@163.com (S. Ding); xzcyg2005@163.com (Y. Chen).