

Phytochemicals from *Inonotus obliquus* and Their Protective Effects Against Diabetic Nephropathy Integrated with Network Pharmacology Analysis

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SUMMARY. Diabetic nephropathy (DN) is one of the severe complications of diabetes mellitus and become the major cause of end-stage renal disease. To find novel therapy for DN, phytochemical investigation on *Inonotus obliquus* has led to the identification of 11 natural compounds. Then we evaluated their protective effects against DN using mesangial cells under high glucose and explored the potential mechanisms using network pharmacology analysis. Among these compounds, compound 5 was found in this plant firstly. *In vitro* evaluation showed most of these compounds could suppress oxidative stress and fibrosis resulting from high glucose in mesangial cells. And *in silico* analysis based on network pharmacology and molecular docking has revealed compounds 1, 2 and 7 could significantly interact with PTP1B and inhibit its activity in cytoplasm, which may be one of potential mechanisms for the phytochemicals in *Inonotus obliquus* targeting 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. Para encontrar una nueva terapia para la DN, la investigación fitoquímica en *Inonotus obliquus* ha llevado a la identificación de 11 compuestos naturales. Luego evaluamos sus efectos protectores contra DN utilizando células mesangiales con niveles altos de glucosa y exploramos los mecanismos potenciales mediante análisis farmacológicos en red. Entre estos compuestos, el compuesto 5 se encontró en primer lugar en esta planta. La evaluación *in vitro* mostró que la mayoría de estos compuestos podrían suprimir el estrés oxidativo y la fibrosis resultantes de los niveles altos de glucosa en las células mesangiales. Y el análisis *in silico* basado en farmacología de redes y acoplamiento molecular ha revelado que los compuestos 1, 2 y 7 podrían interactuar significativamente con PTP1B e inhibir su actividad en el citoplasma, lo que puede ser uno de los mecanismos potenciales para que los fitoquímicos de *Inonotus obliquus* se dirijan a DN.

KEY WORDS: diabetic nephropathy, extracellular matrix, *Inonotus obliquus*, mesangial cells, network pharmacology analysis, oxidative stress.

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