

INTISARI

Latar belakang: Nefropati diabetik adalah komplikasi dari Diabetes Mellitus (DM) akibat hiperglikemia kronis, yang merusak struktur dan fungsi ginjal. Hiperglikemia kronis merusak podosit, mempengaruhi filter glomerulus, dan menyebabkan glomerulosklerosis. Sel tubulus ginjal juga rusak karena peningkatan protein yang melewati tubulus, memicu peradangan dan cedera hingga fibrosis ginjal. *Physalis angulata* adalah tanaman herbal yang memiliki sifat antidiabetes, melindungi pembuluh darah, mengurangi stres oksidatif, dan anti-inflamasi.

Tujuan penelitian: Penelitian ini bertujuan untuk mengetahui efek fraksi aktif *P. angulata* terhadap perkembangan nefropati diabetik.

Metode: Penelitian ini menggunakan fraksi aktif *P. angulata* untuk menguji efeknya pada glukosa darah dan fungsi ginjal. Fraksi aktif dari ekstrak kloroform *P. angulata* diproses dengan metode bioassay-guided. Fraksi aktif merupakan fraksi yang menunjukkan penurunan glukosa tertinggi (26%) dipilih untuk penelitian. Tikus jantan Wistar diinduksi dengan streptozotocin (STZ) untuk mendapatkan model DM. Tikus dibagi dalam lima kelompok berdasarkan dosis fraksi aktif (8,5; 34; dan 136 mg/kgBB). Setelah 2 bulan, ginjal diambil untuk analisis. Glukosa darah diukur secara rutin tiap dua minggu. Urin dikumpulkan untuk analisis mikroalbumin, kreatinin urin, dan klirens kreatinin. qReal-Time PCR digunakan untuk studi ekspresi gen pada SOD1 dan TNF- α . Reverse Transcriptase PCR digunakan untuk studi ekspresi gen seperti SOD2, Nephron, TGF- β , dan vimentin. Cedera tubulus dan glomerulosklerosis dianalisis menggunakan pewarnaan *Periodic Acid Schiff* (PAS), dan fibrosis dianalisis menggunakan pewarnaan sirius red. Ekspresi protein myofibroblast dianalisis menggunakan imunohistokimia dan imunofluoresensi untuk melihat ekspansi α -SMA dan PDGFR- β . Ekspresi protein α -SMA dan PDGFR- β juga dianalisis melalui *western blot*.

Hasil: Hasil penelitian menunjukkan bahwa pemberian *P. angulata* tidak mempengaruhi kadar glukosa darah tikus DM, namun menyebabkan nilai UACR lebih rendah pada dosis tertinggi. Fraksi aktif *P. angulata* nampak mencegah perkembangan glomerulosklerosis, podositopati, stres oksidatif, cedera tubulus, inflamasi, dan fibrosis ginjal. Ekspresi mRNA nefrin, SOD1, SOD2, vimentin, dan TGF- β , serta protein α -SMA dan PDGFR- β mendukung hasil ini.

Kesimpulan: *P. angulata* dapat mencegah perkembangan podositopati, glomerulosklerosis, cedera tubulus, inflamasi, dan fibrosis ginjal pada tikus DM.

Kata kunci: *Physalis angulata* L., Nefropati diabetik, podositopati, glomerulosklerosis, fibrosis.

ABSTRACT

Background: Diabetic nephropathy is a complication of Diabetes Mellitus (DM) caused by chronic hyperglycemia, which damages the structure and function of the kidneys. Chronic hyperglycemia leads to podocyte damage, affecting the glomerular filtration function and causing glomerulosclerosis. Renal tubular cells are also damaged due to increased protein passing through the tubules, triggering inflammation and injury that eventually results in renal fibrosis. *Physalis angulata* is an herbal plant known for its anti-diabetic, vasoprotective, antioxidative, and anti-inflammatory properties.

Objective: This study aims to investigate the effects of the active fraction of *P. angulata* on the progression of diabetic nephropathy.

Methods: This study utilizes the active fraction of *P. angulata* to assess its effects on blood glucose levels and kidney function. The active fraction from the chloroform extract of *P. angulata* was processed using a bioassay-guided method. The fraction showing the highest glucose-lowering effect (26%) was selected for this research. To create a DM model, male Wistar rats were induced with streptozotocin (STZ). The rats were divided into five groups based on the active fraction doses (8.5, 34, and 136 mg/kgBW). After two months, the kidneys were collected for analysis. Blood glucose levels were routinely measured every two weeks. Urine samples were collected to analyze microalbumin, urinary creatinine, and creatinine clearance. Quantitative Real-Time PCR was used to study the gene expression of SOD1 and TNF- α . Reverse Transcriptase PCR was employed to investigate the expression of genes such as SOD2, Nephron, TGF- β , and vimentin. Tubular injury and glomerulosclerosis were analyzed using Periodic Acid Schiff (PAS) staining, while fibrosis was assessed using Sirius red staining. The expression of myofibroblast proteins was examined through immunohistochemistry and immunofluorescence to observe α -SMA and PDGFR- β expansion. Additionally, α -SMA and PDGFR- β protein expression was analyzed via western blotting.

Results: The study's results demonstrate the potential of *Physalis angulata* in preventing the progression of diabetic nephropathy. While the administration of *P. angulata* did not significantly affect blood glucose levels in DM rats, it did lead to lower UACR values at the highest dose. The active fraction of *P. angulata* showed promise in preventing the progression of glomerulosclerosis, podocytopathy, oxidative stress, tubular injury, inflammation, and renal fibrosis. The expression of mRNA for nephron, SOD1, SOD2, vimentin, and TGF- β , as well as the proteins α -SMA and PDGFR- β , supported these findings.

Conclusions: *P. angulata* has the potential to be a significant agent in prevention of the diabetic nephropathy progression in DM rats.

Keywords: *Physalis angulata* L., diabetic nephropathy, podocytopathy, glomerulosclerosis, fibrosis.