

INTISARI

Nefropati diabetik merupakan komplikasi diabetes melitus tipe 2 ditandai dengan penurunan fungsi ginjal progresif akibat stres oksidatif, inflamasi dan fibrosis. Terapi konvensional berfokus pengendalian kadar glukosa darah dan tekanan darah, namun belum sepenuhnya mencegah kerusakan ginjal jangka panjang. Makroalga laut, khususnya *Sargassum cristaefolium* berpotensi sebagai antioksidan, antiinflamasi dan antidiabetes. Kajian menelusuri efek nefroprotektif *S. cristaefolium* melalui jalur PI3K/Nrf2 pada kondisi diabetes masih sangat terbatas, sehingga penelitian ini dilakukan untuk mengisi kesenjangan tersebut.

Penelitian bertujuan meninjau potensi farmakologi makroalga laut Indonesia sebagai terapi antidiabetes serta mengevaluasi efek nefroprotektif fraksi etil asetat ekstrak *S. cristaefolium* pada tikus diabetes melitus tipe 2 melalui mekanisme PI3K/Nrf2. Metode penelitian diawali dengan kajian terhadap hasil-hasil penelitian terkait aktivitas antidiabetes makroalga laut Indonesia guna mengidentifikasi genus makroalga yang paling konsisten dilaporkan memiliki spektrum aktivitas farmakologi antidiabetes yang luas, dilanjutkan uji *in vitro* aktivitas antioksidan DPPH, inhibisi DPP-IV, penetapan kadar fenol dan flavonoid serta identifikasi komponen senyawa dengan GC-MS. Pengujian *in vivo* dilakukan pada tikus Wistar jantan diinduksi diet tinggi lemak dan nikotinamid-streptozotosin. Parameter diamati mencakup kadar glukosa darah, insulin, profil lipid, fungsi ginjal, status antioksidan jaringan, protein ginjal (PI3K, Nrf2, TNF- α , TGF- β) serta gambaran histopatologi ginjal.

Hasil menunjukkan bahwa berbagai makroalga laut Indonesia, terutama dari genus *Sargassum* berpotensi besar sebagai antidiabetes melalui aktivitas antioksidan, antiinflamasi dan perbaikan metabolisme glukosa-lipid. Fraksi etil asetat ekstrak etanol 96% *S. cristaefolium* menunjukkan aktivitas *in vitro* paling kuat dibandingkan ekstrak dan fraksi lainnya dan secara *in vivo* memperbaiki fungsi ginjal, penurunan kadar MDA, peningkatan aktivitas SOD dan kadar GSH serta menginduksi ekspresi jalur PI3K dan Nrf2 diikuti dengan penurunan kadar TNF- α dan TGF- β . Perubahan molekuler berhubungan erat dengan perbaikan struktur histopatologis ginjal dan penurunan rasio berat ginjal. Efek nefroprotektif *S. cristaefolium* dimediasi oleh mekanisme antidiabetes, antioksidan dan antiinflamasi melalui aktivasi jalur PI3K/Nrf2 yang berpotensi sebagai agen nefroprotektif alami pada nefropati diabetik.

Kata kunci: *Sargassum cristaefolium*, nefropati diabetik, PI3K/Nrf2, nefroprotektif.

ABSTRACT

Diabetic nephropathy is a major complication of type 2 diabetes mellitus, characterized by progressive decline in renal function driven by oxidative stress, inflammation, and fibrosis. Current conventional therapies primarily focus on controlling blood glucose levels and blood pressure; However, these approaches have not been fully effective in preventing long-term renal damage. Marine macroalgae, particularly *Sargassum cristaefolium*, has been reported to possess antioxidant, anti-inflammatory, and antidiabetic properties. Nevertheless, studies investigating the nephroprotective effects of *S. cristaefolium* through the PI3K/Nrf2 signaling pathway under diabetic conditions remain limited. Therefore, this study was conducted to address this knowledge gap.

This study aimed to review the pharmacological potential of Indonesian marine macroalgae as antidiabetic agents and to evaluate the nephroprotective effects of the ethyl acetate fraction of *S. cristaefolium* extract in a type 2 diabetes mellitus rat model via the PI3K/Nrf2 pathway. The research methodology began with a review of published studies on the antidiabetic activity of Indonesian marine macroalgae to identify the genus most consistently reported to exhibit a broad spectrum of antidiabetic pharmacological activities. This was followed by in vitro assays, including DPPH radical scavenging activity, DPP-IV inhibition, determination of total phenolic and flavonoid contents, and compound identification using GC-MS. In vivo experiments were conducted in male Wistar rats with type 2 diabetes mellitus induced by a high-fat diet combined with nicotinamide-streptozotocin administration. Observed parameters included blood glucose levels, insulin, lipid profile, renal function, tissue antioxidant status, renal protein expression (PI3K, Nrf2, TNF- α , and TGF- β), and renal histopathological features.

The results demonstrated that several Indonesian marine macroalgae, particularly those of the genus *Sargassum*, exhibit substantial antidiabetic potential through antioxidant and anti-inflammatory activities, as well as improvements in glucose-lipid metabolism. The ethyl acetate fraction of the 96% ethanolic extract of *S. cristaefolium* showed the strongest in vitro bioactivity among all tested extracts and fractions. In vivo, this fraction significantly improved renal function, reduced malondialdehyde (MDA) levels, increased superoxide dismutase (SOD) activity and glutathione (GSH) levels, and induced expression of the PI3K and Nrf2 pathways, accompanied by decreased expression of TNF- α and TGF- β . These molecular alterations were closely associated with improvements in renal histopathological structure and a reduction in the kidney weight ratio. The nephroprotective effects of *S. cristaefolium* are mediated through its antidiabetic, antioxidant, and anti-inflammatory mechanisms via activation of the PI3K/Nrf2 pathway, indicating its potential as a natural nephroprotective agent for diabetic nephropathy.

Keywords: *Sargassum cristaefolium*, diabetic nephropathy, PI3K/Nrf2, nephroprotective.