

Efek Fraksi Aktif Alga Merah *Kappaphycus alvarezii* (Doty) Doty ex P.C Silva terhadap Homeostasis Glukosa Darah pada Tikus Model Diabetik Kajian : Kadar *Glycated Albumin*, *Nε*-(carboxymethyl) lysine, H₂O₂, TNF alpha, Ekspresi gen RAGE (Ager), NADPH oksidase (NOX4) dan NFκB

Abstrak

Hiperglikemia meningkatkan *Advanced Glycation End Products* (AGEs). Interaksinya dengan reseptor, RAGE, menginduksi *Reactive Oxygen Species* (ROS) melalui aktivasi NADPH oksidase, mengaktifkan *Nuclear factor kappa B* (NFκB) dan menyebabkan komplikasi diabetes. *Kappaphycus alvarezii* memiliki senyawa fenolik dan turunannya, termasuk fenol sederhana, flavonoid, *phenols hydroquinone*, triterpenoid, propanoid fenil, tannin, lignin dan zat-zat lain. Potensi alga ini sebagai antiglikasi, antioksidan dan antiinflamasi perlu diteliti lebih lanjut.

Tujuan penelitian ini adalah menentukan fraksi aktif *Kappaphycus alvarezii* dengan kemampuan antiglikasi, mengkaji efeknya terhadap proses glikasi melalui pengukuran kadar *glycated albumin* (GA) dan *Nε*-(carboxymethyl) lysine (CML) plasma serta ekspresi gen RAGE ginjal, stres oksidatif melalui pengukuran H₂O₂ plasma dan ekspresi gen NADPH oksidase (NOX4) ginjal, serta inflamasi melalui pengukuran *Tumor Necrosis Factor alpha* (TNFα) plasma dan ekspresi gen NF-κB ginjal.

Penentuan fraksi aktif menggunakan *Bioassay Guided Fractionation*, terdiri dari, ekstraksi, partisi dan fraksinasi dipandu KLT dan metode BSA-Glukosa untuk memilih fraksi dengan aktivitas antiglikasi (persentase penghambatan dan IC₅₀). Uji *in vivo* menggunakan 20 ekor tikus Wistar jantan (8 minggu, 200 g), terbagi menjadi kelompok non diabetik, diabetik, dan 2 kelompok diabetik dengan pemberian fraksi aktif 11 dan 16,5 mg/kg BB. Pengukuran kadar glukosa plasma dengan GOD-PAP, H₂O₂ plasma dengan spektrofotometri, GA, CML, dan TNFα plasma dengan ELISA. Ekspresi gen RAGE, NOX4 dan NFκB ginjal dianalisis menggunakan RTPCR

Fraksi II memiliki kemampuan antiglikasi tertinggi dan disebut fraksi aktif. Fraksi aktif tidak menurunkan kadar glukosa secara signifikan. Fraksi aktif 11 mg/kg BB secara signifikan menurunkan kadar GA plasma. Fraksi aktif 11 dan 16,5 mg/kg BB secara signifikan menurunkan kadar CML dan H₂O₂ plasma dan menyebabkan ekspresi gen RAGE dan NOX4 ginjal lebih rendah dibandingkan kontrol. Fraksi aktif tidak dapat menurunkan kadar TNFα plasma dan ekspresi gen NFκB ginjal tetap tinggi dibandingkan kontrol.

Kesimpulan penelitian ini adalah fraksi aktif memiliki kemampuan menghambat proses glikasi dan menurunkan stres oksidatif tetapi tidak memiliki kemampuan antiinflamasi.

Kata Kunci : *Kappaphycus alvarezii*, AGEs, RAGE, stres oksidatif, inflamasi

Effect of Red Algae *Kappaphycus alvarezii* (Doty) Doty ex P.C Silva's Active Fraction on Blood Glucose Homeostasis in Diabetic Rat Model Study: Levels of Glycated Albumin, Nε-(carboxymethyl) lysine, H₂O₂, TNF alpha, RAGE (Ager), NADPH oxidase (NOX4) and NFκB gene expression

Abstract

Hyperglycemia increases Advanced Glycation End Products (AGEs). Its interaction with the receptor, RAGE, induces Reactive Oxygen Species (ROS) through activation of NADPH oxidase, activates Nuclear factor kappa B (NFκB) and causes diabetic complications. *Kappaphycus alvarezii* has phenolic compounds and their derivatives, including simple phenols, flavonoids, phenols hydroquinone, triterpenoids, phenyl propanoids, tannins, lignins and other substances. The potential of this algae as antiglycation, antioxidant and anti-inflammatory needs to be investigated further.

The purposes of this study were to determine the active fraction of *Kappaphycus alvarezii* with antiglycation ability, to study its effect on the glycation process by measuring plasma glycated albumin (GA) and Nε-(carboxymethyl) lysine (CML) levels as well as renal RAGE gene expression, oxidative stress by measuring plasma H₂O₂ and renal NADPH oxidase (NOX4) gene expression, and inflammation by measuring plasma Tumor Necrosis Factor alpha (TNFα) and renal NFκB gene expression.

Determination of the active fraction using Bioassay Guided Fractionation, consisting of, extraction, partition and fractionation guided by TLC and BSA-Glucose method to select the fraction with antiglycation activity (percentage of inhibition and IC₅₀). The in vivo test used 20 male Wistar rats (8 weeks, 200 g), divided into non-diabetic, diabetic, and 2 diabetic groups treated with the active fraction 11 and 16.5 mg/kg BW. Measurement of plasma glucose levels by GOD-PAP, plasma H₂O₂ level by spectrophotometry, plasma GA, CML, and TNFα level by ELISA. Renal RAGE, NOX4 and NFκB gene expression were analyzed using RTPCR

Fraction II has the highest antiglycation ability and is called the active fraction. The active fraction did not significantly reduce plasma glucose levels. Active fraction 11 mg/kg BW significantly reduced plasma GA levels. The active fractions 11 and 16.5 mg/kg BW significantly reduced plasma CML and H₂O₂ levels and caused lower renal RAGE and NOX4 gene expressions than control. The active fraction could not reduce plasma TNFα levels and renal NFκB gene expression remained high compared to controls.

The conclusion of this study is the active fraction (fraction II) has the ability to inhibit the glycation process and reduce oxidative stress but has no anti-inflammatory properties.

Keywords: *Kappaphycus alvarezii*, AGEs, RAGE, oxidative stress, inflammation