KAJIAN POTENSI PIGMEN *Spirulina platensis* SEBAGAI KANDIDAT ANTIDIABETES TIPE-2 MENGGUNAKAN SIMULASI *MOLECULAR DOCKING*

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ABSTRAK

Diabetes melitus tipe-2 merupakan penyakit metabolik yang diakibatkan oleh rendahnya kadar insulin sehingga menyebabkan meningkatnya kadar gula darah. Mikroalga *Spirulina platensis* mengandung pigmen feofitin, β-karoten, zeaxantin, dan fikosianobilin yang berpotensi menghambat kerja enzim yang berhubungan dengan diabetes melitus. Pada penelitian ini dilakukan kajian potensi dan mekanisme molekuler beberapa pigmen *Spirulina platensis* sebagai kandidat antidiabetes tipe-2 melalui pendekatan *in silico* menggunakan *docking* molekuler. Simulasi yang dilakukan meliputi penentuan afinitas, interaksi molekuler dan jenis inhibisi antara pigmen terhadap enzim α-amilase, α-glukosidase, dipeptidil peptidase-IV (DPP-IV), dan glukosa-6-fosfat dehidrogenase (G6PD). Tahapan penelitian meliputi preparasi protein, validasi metode *docking*, optimasi dan preparasi ligan, proses *docking*, dan analisis hasil *docking* menggunakan beberapa perangkat lunak diantaranya AutodockTools 1.5.6, AutodockVina 1.1.2, PyMOL 2.4, dan *Discovery Studio Visualization* 2020. Sebagai pembanding digunakan akarbosa, linagliptin dan polidatin. Hasil yang diperoleh menunjukan bahwa afinitas pengikatan pigmen feofitin, β-karoten, dan fikosianobilin dengan α-amilase lebih tinggi berturut-turut 0,4; 2, dan 2,6 *kkal/mol* dari akarbosa. Afinitas pengikatan antara pigmen feofitin, β-karoten, dan fikosianobilin dengan α-glukosidase adalah sama, 1,2, dan 1,6 *kkal/mol* lebih tinggi dari akarbosa. Kompleks antara β-karoten dan fikosianobilin dengan DPP-IV lebih tinggi 0,5 dan 0,3 *kkal/mol* dari linagliptin, serta antara pigmen feofitin, β-karoten, dan fikosianobilin dengan G6PD lebih tinggi 0,2; 1, dan 1,4 *kkal/mol* dari polidatin. Pigmen feofitin, β-karoten, dan fikosianobilin berinteraksi dengan keempat enzim melibatkan ikatan hidrogen, interaksi hidrofobik, gaya van der waals, dan interaksi lainnya. Pigmen feofitin, β-karoten, dan fikosianobilin menginhibisi enzim α-amilase, α-glukosidase, DPP-IV secara kompetitif, dan G6PD secara bukan kompetitif. Berdasarkan hasil simulasi dapat disimpulkan bahwa pigmen feofitin, β-karoten, dan fikosianobilin berpotensi sebagai kandidat antidiabetes. Penelitian empirik perlu dilakukan untuk mengetahui lebih lanjut efektifitas feofitin, β-karoten, dan fikosianobilin sebagai antidiabetes.

Kata kunci : Antidiabetes, Inhibitor enzim, *Molecular docking*, Pigmen *Spirulina platensis*

ABSTRACT

Diabetes mellitus type-2 is a metabolic disease triggered by low insulin production, which causes an increase of blood glucose levels. Microalgae *Spirulina platensis* contains pigments of pheophytin, β-carotene, zeaxanthin, and phycocyanobilin which are potential in inhibiting several enzymes–associated with diabetes mellitus. Here, this study aims to screen the potential and molecular mechanisms of *Spirulina platensis*'s pigments as antidiabetic type-2 candidates through in silico approach using molecular docking. The simulation was analysed the binding affinity, molecular interactions and the type of inhibition among pigments against the enzymes α-amylase, α-glucosidase, dipeptidyl peptidase-IV (DPP-IV), and glucose-6-phosphate dehydrogenase (G6PD). The research stages included protein preparation, validation of the docking method, optimization and preparation of ligands, the docking process, and visualization using several software including AutodockToolsv 1.5.6, AutodockVina 1.1.2, PyMOL 2.4, and Discovery Studio Visualization 2020. The activities of the target compounds were compared to acarbose, linagliptin and polydatin. The results showed that binding affinity of pheophytin, β-carotene, and phycocyanobilin pigments to α-amylase were 0.4, 2, and 2.6 kcal/mol higher than those of acarbose. Binding affinity was also found between pheophytin, β-carotene, and phycocyanobilin pigments with α-glucosidase that reached same affinity, 1.2, and 1.6 kcal/mol higher than acarbose. The complex of β-carotene, and phycocyanobilin pigments 0.5 and 0.3 kcal/mol of linagliptin with DPP-IV, and complex of pheophytin, β-carotene, and phycocyanobilin with G6PD are 0.2, 1, and 1.4 kcal/mol higher from polydatin. Pheophytin, β-carotene, and phycocyanobillin pigments interact with that of four enzymes through hydrogen bonding, hydrophobic interactions, van der waals forces, and other interactions. Pheophytin, β-carotene and phycocyanobilin pigments inhibited α-amylase, α-glucosidase, DPP-IV competitively, and G6PD enzymes not competitively. Based on the simulation, it can be concluded that pheophytin, β-carotene, and phycocyanobilin pigments are potential to be used as antidiabetic candidates. However, experimental research needs to be done for further check the effectiveness of pheophytin, β-carotene and phycocyanobilin as antidiabetic.

Keyword: Antidiabetic, Enzyme inhibitor, *Molecular docking*, *Spirulina platensis*'s pigments

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