PENGEMBANGAN PEPTIDA INHIBITOR α-GLUKOSIDASE DARI HIDROLISAT KASEIN SUSU KAMBING (*Capra hircus*) MELALUI PENDEKATAN *IN-SILICO DIGESTION* DENGAN TRIPSIN DAN PENAMBATAN MOLEKUL

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INTISARI

Peptida bioaktif dari hidrolisis kasein susu kambing berpotensi sebagai obat dalam beberapa penyakit, salah satunya adalah penyakit Diabetes melitus, dengan menginhibisi α-glukosidase. Penelitian ini bertujuan mengidentifikasi urutan asam amino peptida bioaktif inhibitor α-glukosidase dari hidrolisat kasein susu kambing secara *in silico*, kemudian mengoptimasi struktur peptida untuk meningkatkan aktivitas penghambatannya terhadap enzim α-glukosidase.

Kasein susu kambing dihidrolisis melalui *in silico digestion* melalui *server Expasy PeptideMass* dengan tripsin. Peptida yang dihasilkan diidentifikasi bioaktivitasnya dengan *server* dan penambatan molekul digital seperti PeptideRanker, Pepsite2, dan HADDOCK guna mengkaji interaksinya dengan α-glukosidase. Peptida terpilih disintesis dan diuji aktvitas penghambatannya terhadap α-glukosidase untuk memperoleh nilai IC_{50}. Peptida menunjukkan aktivitas penghambatan, kemudian dioptimasi dan dimodifikasi secara *in silico* hingga mendapatkan peptida termodifikasi dengan interaksi dan aktivitas yang paling potensial. Selanjutnya peptida termodifikasi disintesis, diuji aktivitas penghambatannya, ditentukan nilai $IC_{50,}$ serta tipe penghambatannya secara *in vitro*.

Berdasarkan analisis secara *in silico* dan penambatan molekul diperoleh peptida yang paling berpotensi sebagai inhibitor α-glukosidase adalah "EMPFPK" dengan interaksi yang kuat dan stabil terhadap α-glukosidase. Hasil uji aktivitas secara *in vitro* menunjukkan peptida "EMPFPK" berpotensi menginhibisi α-glukosidase dengan nilai IC_{50} sebesar 313,420±1,613 μM. Modifikasi pada peptida "EMPFPK" berhasil dilakukan, peptida termodifikasi "RMPFPR" menunjukkan peningkatan aktivitas penghambatan α-glukosidase yang ditunjukkan dengan interaksi yang lebih kuat dan stabil terhadap triad katalitik Asp215 dan Asp352, serta penurunan nilai IC_{50} menjadi 140,792±1,827 μM dengan tipe penghambatan campuran.

Kata kunci : Diabetes melitus, α-glukosidase, peptida, penambatan molekul

DEVELOPMENT OF α-GLUCOSIDASE INHIBITORY PEPTIDES FROM GOAT MILK (*Capra hircus*) CASEIN HYDROLYSATES THROUGH AN IN SILICO DIGESTION APPROACH USING TRYPSIN AND MOLECULAR *DOCKING*

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ABSTRACT

Bioactive peptides derived from the hydrolysis of goat milk casein have potential as therapeutic agents for various diseases, including diabetes mellitus, by inhibiting α-glucosidase. This study aimed to identify the amino acid sequences of α-glucosidase–inhibitory bioactive peptides from goat milk casein hydrolysates in silico, and to optimize peptide structures to enhance their inhibitory activity against α-glucosidase.

Goat milk casein was hydrolyzed in silico using the Expasy PeptideMass server with trypsin. The resulting peptides were evaluated for bioactivity using digital screening and molecular docking tools such as PeptideRanker, Pepsite2, and HADDOCK to examine their interactions with α-glucosidase. Selected peptides were synthesized and tested for α-glucosidase inhibitory activity to determine their IC_{50} values. Peptides showing inhibitory activity were subsequently optimized and modified in silico to obtain derivatives with the strongest predicted interactions and inhibitory potential. The modified peptides were then synthesized, their inhibitory activities were assessed, IC_{50} values were determined, and their inhibition types were characterized in vitro.

Based on in silico analysis and molecular docking, the peptide “EMPFPK” exhibited the strongest and most stable interaction with α-glucosidase and was identified as the most promising inhibitor. In vitro activity assays showed that “EMPFPK” inhibited α-glucosidase with an IC_{50} value of 313.420 ± 1.613 μM. Structural modification of “EMPFPK” yielded the derivative “RMPFPR” which demonstrated enhanced α-glucosidase inhibitory activity, evidenced by stronger and more stable interactions with the catalytic triad residues Asp215 and Asp352, and reduced IC_{50} value of 140.792 ± 1,827 μM with a mixed-type inhibition.

Keywords : Diabetes mellitus, α-glucosidase, peptide, molecular docking