Pengaruh Pemberian Ekstrak Daun Binahong (Anredera cordifolia (Ten.)Stennis) Terhadap Farmakodinamika dan Farmakokinetika Glibenklamid pada Tikus serta Mekanisme yang Mendasarinya = The Effect of Binahong Leaf Extract (Anredera cordifolia (Ten.) Stennis) Administration on the Pharmacodynamics and Pharmacokinetics of Glibenclamide in Rats, as well as the Mechanisms Underlying It.The Effect of Binahong Leaf Extract (Anredera cordifolia (Ten.) Stennis) Administration on the Pharmacodynamics and Pharmacokinetics of Glibenclamide in Rats, as well as the Mechanisms Underlying It.

Abstrak

Anredera cordifolia (Ten.) Steenis (binahong) merupakan salah satu bahan alam yang memiliki potensi dan digunakan untuk pengobatan tradisional. Efek farmakologi tanaman binahong dapat digunakan sebagai alternatif menurunkan kadar glukosa darah. Penelitian terdahulu melaporkan bahwa penggunaan bersama herbal dengan obat sintetik dapat menyebabkan terjadi perubahan pada farmakodinamika dan farmakokinetika obat sintetik. Informasi mengenai interaksi antara obat herbal dengan obat sintetik masih terbatas sehingga perlu diketahui efektivitas penggunaan kombinasi tersebut. Penelitian ini bertujuan untuk membuktikan adanya interaksi farmakodinamika dan farmakokinetika kombinasi ekstrak daun binahong dengan glibenklamid yang diberikan secara oral sebagai antidiabetes. Penelitian ini dilakukan secara ekperimental dan non ekperimental. Penelitian eksperimental dibagi menjadi dua bagian. Bagian pertama adalah pengujian interaksi farmakodinamika untuk efek antidiabetes dengan metode pengukuran kadar glukosa secara enzimatik. Kadar glukosa darah diukur sebelum perlakuan, setelah induksi pakan tinggi lemak (sukrosa 20 %, lemak sapi 20 %, mentega 10% dan pakan standar 50 %) dan setelah pemberian sediaan uji. Pengambilan sampel darah digunakan untuk pengujian TTGO, profil asam amino dan profil asam lemak. Bagian kedua adalah pengujian interaksi farmakokinetika dengan mengambil darah tikus pada titik tertentu setelah pemberian ekstrak daun binahong dan obat glibenklamid. Konsentrasi glibenklamid diukur dengan menggunakan kromatografi cair kinerja ultra tinggi-tandem spektrometri massa (KCKUT-SM/SM), selanjutnya dihitung nilai AUC, Tmaks, Cmaks, T1/2 dan Ke. Penelitian non ekperimental dilakukan drug design untuk memprediksikan ikatan antara kandidat molekul obat glibenklamid dan vitexin (senyawa yang terdapat dalam ekstrak binahong) sebagai antidiabetes dengan protein target CYP3A4 secara in silico dengan menggunakan molecular docking serta memprediksi interaksi antarprotein. Hasil uji pada farmakodinamika diperoleh kadar glukosa darah pada kombinasi glibenklamid (4,5 mg/kgBB) dengan ekstrak daun binahong dosis 1 (17,5 mg/kgBB), dosis 2 (35 mg/kgBB) dan dosis 3 (70mg/kgBB) dapat menurunkan kadar glukosa darah kembali normal namun persentase penurunan kadar glukosa pada hari ke 21 terbesar terdapat pada kelompok kontrol positif. Pada pengujian tes toleransi glukosa kelompok kombinasi memperoleh nilai AUC sebanding dengan nilai AUC kelompok positif yang diberi glibenklamid. Hasil penelitian pada profil asam lemak dan profil asam amino menunjukkan kelompok kombinasi obat dengan ekstrak daun binahong mengalami penurunan asam lemak dan peningkatan asam amino. Hasil uji profil farmakokinetika glibenklamid berbeda antara pemberian tunggal dengan kombinasi ekstrak daun

binahong. Pemberian glibenklamid (4,5 mg/kgBB) dengan ekstrak daun binahong (70mg/kgBB) dapat menurunkan AUC dan Cmaks serta memperpanjang Tmaks. Hasil energi bebas gibs (G) pada molecular docking diperoleh nilai glibenklamid dan vitexin yang berikatan dengan reseptor CYP3A4 dengan score ChemPLP sebesar -4,4 kkal/mol, glibenclamid dengan reseptor -3,2 kkal/mol dan vitexin dengan reseptor yaitu -3,2 kkal/mol, dapat disimpulkan bahwa pemberian kombinasi glibenklamid (4,5 mg/kgBB) dengan ekstrak daun binahong dosis 1 (17,5 mg/kgBB), dosis 2 (35 mg/kgBB) dan dosis 3 (70mg/kgBB) secara oral dapat menurunkan kadar glukosa darah pada tikus yang diinduksi pakan tinggi lemak. Persentase penurunan kadar glukosa darah lebih tinggi pada kelompok yang hanya diberikan glibenklamid 4,5 mg/kgBB (kelompok positif), sementara pada kelompok pemberian tunggal (ekstrak binahong dosis 1,2 dan 3), mengalami penurunan kadar glukosa tetapi tidak lebih tinggi persentase penurunan kadar glukosa darah dibandingkan dengan kelompok kontrol positif. Pada uji farmakokinetika pemberian kombinasi glibenklamid (4,5 mg/kgBB) dengan ekstrak daun binahong (70 mg/kgBB) secara oral dapat menurunkan kadar obat glibenklamid dalam plasma tikus.

.....Anredera cordifolia (Ten.) Steenis (binahong) is a natural ingredient with potential and is used in traditional medicine. The pharmacological effect of the binahong plant can be used as an alternative to lower blood glucose levels. Previous studies have reported that the concomitant use of herbs with synthetic drugs can cause changes in the pharmacodynamics and pharmacokinetics of synthetic drugs. Information regarding the interaction between herbal medicines and synthetic drugs is still limited, so it is necessary to know the effectiveness of using these combinations. This study aims to prove the pharmacodynamic and pharmacokinetic interactions of the combination of binahong leaf extract with glibenclamide administered orally as an anti-diabetic. This research was conducted experimentally and non-experimentally. Experimental research is divided into two parts. The first step is to test the pharmacodynamic interactions for the anti-diabetic effect using the enzymatic method of measuring glucose levels. Blood glucose level pressure was measured before treatment, after induction of a high-fat diet (20% sucrose, 20% beef fat, 10% butter, and 50% standard feed), and after administration of the test preparation. Blood sampling was used for testing OGTT, the amino acid profile, and the fatty acid profile. The second part is testing pharmacokinetic interactions by taking rat blood at a certain point after administration of binahong leaf extract and glibenclamide drug. The concentration of glibenclamide was measured using ultra-high performance liquid chromatography-tandem mass spectrometry (KCKUT-SM/SM), then the AUC, Tmax, Cmax, T1/2, and Ke values were calculated. Non-experimental research was conducted with drug design to predict the bond between candidate drug molecules glibenclamide and vitexin, one of the compounds contained in binahong extract as an anti-diabetic with CYP3A4 target protein in silico, by using molecular docking and predicting interactions between proteins. The results of the pharmacodynamic test obtained blood glucose levels in the combination of glibenclamide (4.5 mg/kg BW) with binahong leaf extract dose 1 (17.5 mg/kg BW), dose 2 (35 mg/kg BW), and dose 3 (70mg/kg BW) can reduce blood glucose levels back to normal, but the percentage of decrease in glucose levels on the 21st day is greatest in the positive control group. In the glucose tolerance test, the combined group obtained an AUC value comparable to the one in the positive group given glibenclamide. The study's results on the fatty acid profile and amino acid profile showed that the combination group of drugs with binahong leaf extract experienced a decrease in fatty acids and an increase in amino acids. The test results of the pharmacokinetic profile of glibenclamide were different between a single administration and a combination of binahong leaf extract. Giving glibenclamide (4.5 mg/kg BW) with binahong leaf extract (70mg/kg BW) can reduce AUC and Cmax and prolong Tmax. The

results of gibs free energy (G) on molecular docking obtained the values of glibenclamide and vitexin, which bind to the CYP3A4 receptor with a ChemPLP score of -4.4 kcal/mol, glibenclamide with a receptor -3.2 kcal/mol and vitexin with a receptor of-3,2 kcal/mol. Conclusion The results of this study show that the administration of a combination of glibenclamide (4.5 mg/kg BW) with binahong leaf extract dose 1 (17.5 mg/kg BW), dose 2 (35 mg/kg BW) and dose 3 (70mg/kg BW) orally can lower blood glucose levels in rats induced by a high-fat diet, but the percentage reduction in blood glucose levels was better in the group that was only given glibenclamide 4.5 mg/kgBW (positive group), while in the group that was only given binahong extract doses of 1,2 and 3 also experienced a decrease in glucose levels but the percentage decrease in glucose levels was not greater than the positive control group. In the pharmacokinetic test orally administering a combination of glibenclamide (4.5 mg/kg BW) with binahong leaf extract (70 mg/kg BW) can reduce glibenclamide drug levels in rat plasma with binahong leaf extract (70 mg/kg BW) can reduce glibenclamide drug levels in rat plasma