

INTISARI

Penggunaan bahan alam bersama obat ditujukan untuk meningkatkan efektivitas pengobatan. Penggunaan obat bersama dengan bahan alam berpotensi menimbulkan interaksi farmakokinetik dan farmakodinamik. Penelitian ini ditujukan untuk menetapkan pengaruh ekstrak etanol bekatul beras hitam (EEBBH) terhadap efektivitas glibenklamid (Gli) sebagai antihiperglikemik dan potensi interaksi farmakokinetiknya.

Penelitian didahului dengan penetapan kadar antosianin total dalam ekstrak dengan metode perbedaan pH. Ekstrak yang telah diketahui kadar antosianin totalnya diujikan pada 35 ekor tikus jantan wistar yang dibagi secara random untuk studi farmakodinamik dan farmakokinetik. Perlakuan selama 28 hari dilakukan setelah induksi dengan aloksan 150 mg/kgBB secara intraperitoneal berhasil menaikkan kadar gula darah puasa (GDP) >200 mg/dL pada hari ke-5. Perlakuan pada 5 ekor tikus tiap kelompok diberikan secara peroral dengan sediaan sebagai berikut: kelompok normal, aloksan 150 mg/kgBB, Gli 5 mg/kgBB, EEBBH 50 mg/kgBB dan Gli 5+EEBBH 50 mg/kgBB. Pemantauan aktivitas farmakodinamik dilakukan terhadap parameter: kadar GDP, kadar insulin serum, kadar glikogen hati, ekspresi GLUT4 di jaringan otot skelet dan sel adiposa. Uji histopatologi diamati pada organ pankreas, hati dan ginjal untuk pemantauan kerusakan sel. Pemantauan fase farmakokinetik dilakukan terhadap 10 ekor tikus hiperglikemik yang dibagi dalam 2 kelompok, yaitu kelompok Gli dan kelompok Gli+BBH. Parameter yang dibandingkan adalah K_a , $C_{p_{maks}}$, t_{maks} , AUC, MRT, V_D , $t_{1/2}$ dan Cl_T diolah menggunakan software PK Solver. Analisis data dengan statistik parametris dan nonparametris menggunakan software SPSS versi 23.

Hasil penelitian menunjukkan bahwa EEBBH yang mengandung kadar antosianin total sebesar $(29,27 \pm 0,69)$ mg%b/b ini akan bersinergi dengan Gli dalam menurunkan kadar GDP dan meningkatkan sekresi insulin serum, ekspresi dan translokasi GLUT4 di jaringan adiposa serta perbaikan sel di organ pankreas, hati dan ginjal. Pemberian EEBBH tidak mempengaruhi kemampuan Gli dalam meningkatkan kadar glikogen hati dan ekspresi GLUT4 di jaringan otot skelet. Profil farmakokinetik Gli pada fase absorpsi, distribusi dan eliminasi tidak dipengaruhi oleh EEBBH baik yang diberikan tunggal maupun berulang. Berdasarkan hasil dapat disimpulkan bahwa EEBBH mampu meningkatkan efektivitas Gli sebagai antidiabetes tanpa mempengaruhi profil farmakokinetiknya.

Kata kunci: ekstrak etanol bekatul beras hitam, Glibenklamid, kadar gula darah, kadar insulin serum, ekspresi GLUT4

ABSTRACT

The use of natural ingredients with drugs is intended to increase the effectiveness of treatment. However, the use of drugs together with natural ingredients has the potential to cause pharmacokinetic and pharmacodynamic interactions. This study was aimed to determine the effect of ethanolic extract of black rice bran (EEBRB) on the effectiveness of Gli as an antihyperglycemic agent and its potential pharmacokinetic interactions.

The study was preceded by the determination of total anthocyanin levels in the extract using the pH difference method. Extracts with predetermined total anthocyanin levels were tested on 35 male rats for pharmacodynamic and pharmacokinetic studies. Treatment for 28 days was carried out after induction with alloxan 150 mg/kgBW intraperitoneally in rats with fasting blood glucose levels (FBG) more than 200 mg/dL on day 5. The treatment of 5 rats in each group was given orally respectively: normal group, alloxan 150 mg/kgBW, Gli 5 mg/kgBW, EEBRB 50 mg/kgBW and Gli 5+EEBRB 50 mg/kgBW. Monitoring of pharmacodynamic activity was carried out on parameters: fasting blood glucose (FBG) levels, serum insulin levels, liver glycogen levels, GLUT4 expression in skeletal muscle tissue and adipose cells. Histopathological tests were observed on the pancreas, liver and kidneys to monitor cell damage. The results showed that EEBRB had an effect on the effectiveness of reducing FBG levels, increasing serum insulin secretion, GLUT4 expression and translocation in adipose tissue and cell repair in the pancreas, liver and kidneys. Pharmacokinetic phase monitoring was carried out on 10 hyperglycemic rats which were divided into 2 groups: the Gli group and the Gli+BRB group. The parameters evaluated were K_a , C_{pmax} , t_{max} , AUC, MRT, V_D , $t_{1/2}$ and CL_T processed using PK Solver software. Data analysis with parametric and non-parametric statistics using SPSS version 23 software.

The results showed that EEBRB containing total anthocyanin levels of (29.27 ± 0.69) mg% w/w will synergize with Gli in reducing FBG levels and increasing serum insulin secretion, GLUT4 expression and translocation in adipose tissue and cell repair in pancreas, liver and kidney organs. The administration of EEBRB did not affect the ability of Gli to increase liver glycogen levels and GLUT4 expression in skeletal muscle tissue. The pharmacokinetic profile of Gli in the absorption, distribution and elimination phases was not affected by EEBRB, whether given alone or repeatedly. Based on the results, it can be concluded that EEBRB were able to increase the effectiveness of Gli as an antidiabetic without affecting its pharmacokinetic profile.

Keywords :ethanolic extract of black rice bran, Glibenclamide, blood sugar levels, serum insulin levels, GLUT4 expression