

ABSTRAK

Diabetes melitus tipe 2 (DMT2) memiliki angka morbiditas dan mortalitas terus meningkat yang merupakan penyebab kematian tertinggi ketiga dunia setelah stroke dan penyakit kardiovaskular. Indonesia berada pada urutan keenam insiden DMT2 tahun 2021. Pengobatan standar DMT2 saat ini diantaranya dengan obat oral, tapi efek samping obat tersebut sering merugikan bagi penderita, sehingga diperlukan alternatif terapi yang memiliki efek samping minimal. Ekstrak etanol asam gelugur (EAG) merupakan obat bahan alam yang sebelumnya dijadikan obat antiobesitas dan berpotensi menurunkan kadar glukosa darah pada DMT2. Tujuan penelitian ini adalah menganalisis pengaruh EAG terhadap glukosa darah, massa otot soleus, ekspresi gen *mRNA PI3K* dan *GLUT4* otot soleus tikus DMT2.

Metodologi penelitian eksperimental, menggunakan tikus jantan galur *Wistar* spesies *R. norvegicus* berumur 8–12 minggu sebanyak 20 ekor. Tikus secara random dikelompokkan menjadi empat kelompok, setiap kelompok terdiri dari lima ekor yaitu kelompok normal (N), kelompok normal+EAG (N+EAG), kelompok diabetes melitus tipe 2 (DMT2), dan kelompok diabetes melitus tipe 2 yang diberikan EAG (DMT2+EAG). Model tikus DMT2 diinduksi dengan STZ 50 mg/kg BB sekali penyuntikan. Pemberian EAG 400 mg/kg BB satu kali setiap hari selama empat minggu. Jaringan otot soleus diambil dan ditimbang pada akhir penelitian dan digunakan untuk pemeriksaan *mRNA PI3K* dan *GLUT4* menggunakan metode RT-PCR. Kadar glukosa darah pada akhir penelitian diambil dari ekor tikus. Data dianalisis dengan uji *one way ANOVA* dan dilanjutkan dengan uji *Post Hoc Tukey* atau *Games Howell*.

Hasil penelitian menunjukkan EAG menurunkan kadar glukosa darah puasa secara signifikan antara kelompok DMT2 sebesar 523 mg/dl dibanding dengan kelompok DMT2+EAG sebesar 311 mg/dL ($p=0,000$). Massa otot soleus tidak menunjukkan perbedaan signifikan antara kelompok DMT2 dengan DMT2+EAG, masing-masing 0,240 gram dan 0,282 gram ($p=0,403$). Ekspresi gen *mRNA PI3K* mengalami perbedaan antara kelompok DMT2 dengan kelompok DMT2+EAG masing-masing sebesar 0,321 AU dan 0,497 AU ($p=0,003$). Ekspresi gen *mRNA GLUT4* menunjukkan perbedaan yang signifikan antara kelompok DMT2 dengan DMT2+EAG masing-masing sebesar 1,269 AU dan 2,288 AU ($p=0,018$).

Simpulan penelitian EAG 400 mg/kg BB yang diberikan setiap hari selama empat minggu dapat menurunkan kadar glukosa darah, meningkatkan ekspresi *mRNA PI3K* dan *mRNA GLUT4*, namun tidak meningkatkan massa otot soleus. Penelitian yang akan datang diperlukan untuk menganalisis pengaruh EAG terhadap ekspresi gen selain di otot soleus dan pemeriksaan massa otot lain terutama gastroknemius, serta studi tentang pengukuran translokasi GLUT4 melalui pemeriksaan *High performance liquid chromatography* (HPLC).

Kata kunci: ekstrak etanol asam gelugur, glukosa darah, massa otot soleus, *mRNA PI3K*, *mRNA GLUT4*, streptozotisin

ABSTRACT

Type 2 diabetes mellitus (DMT2) has continuously increasing morbidity and mortality rates which is the third leading cause of death in the world after stroke and cardiovascular disease. Indonesia is in sixth place for the incidence of DMT2 in 2021. Currently, the standard

treatment for DMT2 includes oral drugs, but the side effects of these drugs are often detrimental to sufferers, so alternative therapies are needed that have minimal side effects. The ethanol extract of asam gelugur (EAG) is a natural product that was previously used as an anti-obesity drug and has the potential to reduce blood glucose levels in T2DM. The purpose of this study was to analyze the effect of EAG on blood glucose, soleus muscle mass, PI3K, and GLUT4 mRNA gene expression of the soleus muscle of DMT2 rats.

Experimental research methodology, using 20 male Wistar strain *R. norvegicus* male rats aged 8–12 weeks. Mice were randomly grouped into four groups, each group consisting of five rats, namely the normal group (N), the normal+EAG group (N+EAG), the type 2 diabetes mellitus (DMT2) group, and the type 2 diabetes mellitus group which was given EAG (DMT2+EAG). The DMT2 rat model was induced with STZ 50 mg/kg BW once. Giving EAG 400 mg/kg BW once a day for four weeks. Soleus muscle tissue was taken and weighed at the end of the study and used for PI3K and GLUT4 mRNA examination using the RT-PCR method. Blood glucose levels at the end of the study were taken from rats. Data were analyzed by one way ANOVA test and followed by Tukey's or Games Howell's Post-Hock test.

The results showed that EAG significantly reduced fasting blood glucose levels between the T2DM group by 523 mg/dl compared to the DMT2+EAG group by 311 mg/dL ($p=0.000$). Soleus muscle mass did not show a significant difference between the DMT2 and DMT2+EAG groups, 0.240 gram and 0.282 gram respectively ($p=0.403$). The expression of the PI3K mRNA gene was different between the DMT2 group and the DMT2+EAG group, respectively 0.321 AU and 0.497 AU ($p=0.003$). GLUT4 mRNA gene expression showed a significant difference between the DMT2+EAG group of 1.269 AU and 2.288 AU respectively ($p=0.018$).

Conclusion: EAG 400 mg/kg BW given daily for four weeks can reduce blood glucose levels, and increase the expression of PI3K mRNA and GLUT4 mRNA, but not increase soleus muscle mass. Future research is needed to analyze the effect of EAG on gene expression other than in the soleus muscle and examination of other muscle masses, especially the gastrocnemius, as well as studies on measuring GLUT4 translocation through High performance liquid chromatography (HPLC) examination.

Keywords: gelugor acid ethanol extract, blood glucose, soleus muscle mass, PI3K, GLUT4, streptozotocin