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**Efek Ekstrak Daun Mahkota Dewa (Phaleria Macrocarpa Scheff Boerl.) terhadap Jumlah Makrofag M1 Pulau
Langerhans Model Tikus Diabetes**
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INTISARI

Efek Ekstrak Daun Mahkota Dewa (*Phaleria Macrocarpa* Scheff Boerl.) terhadap Jumlah Makrofag M1 Pulau Langerhans Model Tikus Diabetes

Latar Belakang: Diabetes mellitus (DM) merupakan salah satu penyebab utama kematian dan disabilitas di seluruh dunia. Patogenesis DM berkaitan erat dengan proses inflamasi pada pulau Langerhans yang dimediasi oleh makrofag. Terdapat dua jenis aktivasi dan fungsi makrofag, yakni makrofag M1 (pro-inflamasi) dan makrofag M2 (anti-inflamasi). Pada DM, aktivasi makrofag M1 memicu reaksi inflamasi, resistensi insulin, penurunan sekresi insulin dan disfungsi sel β pada pulau Langerhans sehingga menyebabkan kondisi hiperglikemia kronis. Daun mahkota dewa mengandung senyawa flavonoid, alkaloid, saponin, polifenol, dan senyawa aktif phalerin. Beberapa senyawa ini memiliki efek anti-inflamasi dan antioksidan sehingga berpotensi untuk mempengaruhi polarisasi makrofag pada kasus DM.

Tujuan: Mengkaji pengaruh pemberian ekstrak daun mahkota dewa (*Phaleria macrocarpa* Scheff Boerl.) terhadap jumlah makrofag M1 pulau Langerhans tikus model diabetes.

Metode: Penelitian kuasi-eksperimental dengan desain *post-test only group* ini menggunakan subyek tikus putih (*Rattus novergicus*) galur *Sprague-Dawley* jantan berusia 8 minggu yang diinduksi diabetes dengan menggunakan *streptozotocin* (STZ) dan *nicotinamide* (NA). Tikus dibagi ke dalam 3 kelompok, yakni kelompok kontrol non-diabetes, kelompok kontrol diabetes yang diberi pelarut dan kelompok diabetes yang diberi ekstrak etanol daun mahkota dewa (EEDMD) dengan dosis 14 mg/200g per oral 1 kali sehari. Tikus diterminasi pada hari ke-14 dan 25 pemberian ekstrak. Jaringan pankreas diisolasi kemudian dibuat preparat yang diwarnai dengan antibodi anti-iNOS. Jumlah sel immunopositif dihitung dengan menggunakan *ImageJ* dan *H Score*.

Hasil: Rerata jumlah makrofag M1 pulau Langerhans hari ke-14 tidak dapat dianalsis secara statistik karena banyaknya pankreas yang rusak. Rerata jumlah makrofag M1 pulau Langerhans antarkelompok hari ke-25 tidak berbeda secara signfikan.

Kesimpulan: Jumlah sel immunopositif pulau Langerhans model tikus diabetes yang diberi EEDMD lebih banyak dibandingkan jumlah sel immunopositif pulau Langerhans model tikus diabetes yang tidak diberi EEDMD, tetapi tidak signifikan secara statistik.

Kata kunci: diabetes mellitus, makrofag M1, daun mahkota dewa

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ABSTRACT

Effect of Mahkota Dewa (*Phaleria Macrocarpa* Scheff Boerl.) Leaf Extract on the Number of Islets of Langerhans' M1 Macrophage in Diabetic Rat Model

Background: Diabetes mellitus (DM) is one of the leading causes of death and disabilities around the world. The pathogenesis of DM is closely linked to inflammatory processes in the islets of Langerhans mediated by macrophages. There are two subsets of macrophages based on their activities and functions, namely M1 (pr-inflammation) and M2 (anti-inflammation) macrophages. In DM, the activation of M1 macrophages induces inflammation, insulin resistance, decrease in insulin production and β cells dysfunction which lead to chronic hyperglycemia. Mahkota dewa leaves are known to contain flavonoid, alkaloid, saponin, polyphenols and *phalerin*. Some of these substances have anti-inflammatory and anti-oxidant activities which may have potential effect in the polarization of macrophages during the course of the disease.

Objective: To evaluate the effects of mahkota dewa leaves (*Phaleria macrocarpa* Scheff Boerl.) extract on the number of islets of Langerhans' M1 macrophages in diabetic rat model.

Method: This was a quasi-experimental study with post-test only group design. Male Sprague Dawley rats age 8 weeks were made diabetic by the administration of streptozotocin (STZ) and nicotinamide (NA). The subjects were divided into 3 different groups, namely non-diabetic control group, diabetic control group with solvent, and diabetic group given 14mg/200g ethanolic extract of mahkota dewa leaves (EEMDL) per oral once a day. The rats were terminated on the 14^{th} and 25^{th} day of extract administration. Pancreas were then isolated and made into paraffin blocks. The slide samples were stained with immunohistochemistry (IHC) anti-iNOS antibody. The number of immunopositive cells was recorded using ImageJ and H Score.

Results: The mean number of islets of Langerhans' M1 macrophages of the groups terminated on day 14 were not analyzed statistically due to the massive destruction of normal pancreatic structures in most samples. The mean number of islets of Langerhans' M1 macrophages between groups terminated on day 25 were not significantly different.

Conclusion: The number of immunopositive cells in the islets of Langerhans of diabetic rats that were treated with EEMDL was higher than the number of immunopositive cells in the islets of Langerhans of diabetic rats that were not treated with EEMDL, although the differences were not statistically significant.

Keywords: diabetes mellitus, M1 macrophage, mahkota dewa