Efek pemberian mangiferin dibandingkan dengan pioglitazon terhadap resistensi insulin pada tikus yang diinduksi dengan diit tinggi fruktosa = Effect of mangiferin versus pioglitazon against insulin resistance in rats induced by high fructose diet

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Abstrak

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Latar Belakang: Mangiferin (MGR) adalah glikosida xanton yang pertama kali diisolasi dari Mangifera indica. Efek anti hiperglikemik dan anti hiperlipidemik MGR merupakan akibat dari aktivasi peroxisome proliferator activated gamma (PPAR) dan AMP-activated protein kinase (AMPK). Aktivasi PPAR menyebabkan peningkatan transkripsi gen glucose transporter 4 (GLUT4) sedangkan aktifasi AMPK menyebabkan stimulasi translokasi GLUT4 ke membran sel serta peningkatan oksidasi asam lemak. Mekanisme tersebut sama dengan tiazolidinedion (TZD), yaitu obat yang digunakan untuk pengobatan resistensi insulin.

Metode: Tikus Spraque Dawley jantan diinduksi resistensi insulin selama 6 minggu dengan memberikan larutan fruktosa 60% melalui sonde dan fruktosa 10% sebagai air minum. Setelah induksi resistensi insulin selesai dilakukan terapi dengan MGR 50 mg/kgBB/hari atau MGR 100 mg/kgBB/hari atau pioglitazon (PIO) 3 mg/kgBB/hari diberikan selama 4 minggu dan selama itu induksi fruktosa tetap dilakukan. Pemeriksaan kadar glukosa, trigliserida, insulin, dan perhitungan nilai HOMA-IR dilakukan pada akhir minggu ke-6 sedangkan kadar kolesterol total plasma puasa, kadar protein kinase C alfa otot, serta tingkat ekspresi mRNA GLUT4 otot dan lemak diperiksa pada akhir minggu ke-10.

Hasil: Pada tikus dengan resistensi insulin yang mendapatkan MGR 50 mg/kgBB/hari dan MGR 100 mg/kgBB/hari terdapat kecenderungan penurunan kadar trigliserida dan kolesterol total puasa, sedangkan kecenderungan penurunan kadar glukosa dan insulin puasa serta nilai HOMA-IR ditemukan pada kelompok yang mendapatkan MGR 50 mg/kgBB/hari bila dibandingkan dengan kelompok yang tidak mendapatkan terapi (IND FRK). Pada kelompok yang mendapatkan PIO 3 mg/kgBB/hari terdapat penurunan kadar glukosa, trigliserida, insulin, kolesterol total puasa, dan nilai HOMA-IR yang berbeda bermakna dengan kelompok IND FRK. Peningkatan ekspresi mRNA GLUT4 pada jaringan otot dan lemak terlihat pada kelompok yang mendapatkan MGR dan PIO, dan peningkatan ekspresi tersebut sedikit lebih besar pada kelompok yang mendapatkan PIO. Pada pemeriksaan kadar PKC tidak ditemukan adanya perbedaan yang bermakna di semua kelompok.

Kesimpulan: Pada penelitian ini dapat disimpulkan bahwa pemberian MGR 50 mg/kgBB memiliki potensi untuk memperbaiki resistensi insulin meskipun perbaikan tersebut masih belum optimal dibandingkan dengan kelompok yang mendapatkan PIO 3 mg/kgBB/hari.
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ABSTRACT

Introduction: Mangiferin (MGR) is a glucoside xanthone that is first isolated from Mangifera indica. Anti-hyperglycemic and anti-hiperlipidemic effect of mangiferin related to activation of peroxisome proliferator activated gamma (PPAR) and AMP-activated protein kinase (AMPK). Mangiferin act as PPAR agonist and activate glucose transporter 4 (GLUT4) gene transcription while activation of AMPK leads to GLUT4 translocation to cell membrane and fatty acids oxidation. This mechanism are same as tiazolidinedion (TZD), which is one of medicine used for insulin resistance treatment.

Methode: Male Spraque-Dawley rats are fed with high fructoce concentration (60% on direct oral and 10% in drinking water) for 6 weeks (IND FRK) to induced insulin resistance. Treatment with MGR 50 mg/kgBW/day or 100 mg/kgBW/day or pioglitazone (PIO) 3 mg/kgBW/day is given for 4 weeks after insulin resistance induction. Fasting plasma glucose, triglyceride, insulin, and HOMA-IR value are measured in the end of sixth and tenth week. Fasting plasma total cholesterol, muscle protein kinase C (PKC) level, and mRNA GLUT4 expression level in muscle and white adipose tissue are measured in the end of tenth week.

Result: In this study we found that MGR 50 mg/kgBW and MGR 100 mg/kgBW had tendention to decreased fasting plasma triglyceride and total cholesterol, while MGR 50 mg/kgBW/day also had tendention to decreaced fasting plasma glucose and insulin, and HOMA-IR value. In PIO treated rats, there were significant decreasement of fasting plasma glucose, triglyceride, insulin, and total cholesterol, and HOMA-IR value compared with untreated rats. Increase expression level of mRNA GLUT4 in muscle and adipose tissue were observed in rats given MGR 50 and 100 mg/kgBW/day and PIO 3 mg/kgBW/day. Expression level of muscle and adipose mRNA GLUT4 in PIO treated rats were higher than in MGR treated rats. In all study groups there were no significant difference of muscle PKC level.

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