Efek Modulasi 6-Gingerol Pada Model Tikus Sindrom Metabolik: Fokus Pada Jalur Endoplasmic Reticulum Stress = Modulation Effect of 6-Gingerol In Metabolic Syndrome Rats by Regulating Endoplasmic Reticulum Stress Pathway

Shirly Gunawan, author

Abstrak

Latar Belakang: Sindrom metabolik (MetS) melibatkan endoplasmic reticulum stress (ER stress) di dalam patogenesisnya. 6-gingerol diketahui memiliki banyak efek farmakologi yang berpotensi untuk pengobatan MetS. Studi ini bertujuan untuk meneliti efek modulasi 6-gingerol terhadap MetS melalui jalur ER stress dan menentukan dose-response relationship.
Metode: Pembuatan model MetS menggunakan tikus Sprague-Dawley jantan yang diberikan diet high-fat high fructose (HFHF) selama 16 minggu dan diinjeksi streptozotocin intraperitoneal dosis 22 mg/kgBB pada minggu ke-8. Dua puluh lima ekor tikus dibagi menjadi kelompok diet standar, kontrol negatif (HFHF) dan 3 kelompok perlakuan yang masing-masing diberikan 6-gingerol dosis 50, 100 dan 200 mg/kgBB selama 8 minggu. Setelah tikus dikorbankan, dilakukan pemeriksaan kadar glukosa darah puasa, HOMA-IR, kolesterol total, HDL, LDL, trigliserida; serta parameter ER stress yaitu GRP78 dan IRE1, serta pemeriksaan histopatologik hati.
Hasil: Hasil studi menunjukkan 6-gingerol dapat mengurangi berat badan, menurunkan glukosa darah puasa, memperbaiki resistensi insulin, menurunkan kadar kolesterol total, LDL dan trigliserida serta mengurangi secara signifikan akumulasi lipid dan apoptosis hepatosit ($p<0,05$). Perbaikan terhadap kelainan metabolik tersebut terjadi melalui downregulasi ekspresi protein GRP78 dan IRE1 pada pemberian dosis 200mg/kgBB secara bermakna ($p<0,05$).
Kesimpulan: Studi ini berhasil membuktikan efek modulasi 6-gingerol pada sindrom metabolik secara dose-dependent melalui jalur ER stress.
.....Background: Metabolic syndrome (MetS) implicates ER stress in its pathogenesis. 6-gingerol is known to have many potential pharmacological effects for treating MetS. This study aims to investigate the modulating effect of 6-gingerol on MetS via the ER stress pathway and determine the dose-response relationship.

Methods: To induce MetS, male Sprague-Dawley rats were fed high-fat high fructose (HFHF) diet for 16 weeks and injected with low-dose intraperitoneal streptozotocin (22 mg/kg BW) at week 8. Twenty-five rats were divided into a standard diet group, negative control (HFHF), and three treatment groups with 6-gingerol doses of 50, 100, and 200 mg/kg BW for eight weeks, respectively (given after eight weeks of induction). At the end of the study, all rats were sacrificed. Then the following tests were carried out, including fasting blood glucose, HOMA-IR, total cholesterol, HDL, LDL, and triglyceride levels; and ER stress parameters (GRP78 and IRE1), also a histopathological examination of liver.
Results: 6-gingerol can reduce body weight, lower fasting blood glucose and improve insulin resistance, reduce total cholesterol, LDL, and triglyceride levels, and significantly reduced lipid accumulation and apoptosis in hepatocytes ($p<0,05$). Improvement of these metabolic abnormalities occurred through

downregulation of GRP78 protein expression, IRE1 (dose of 200 mg/kgBW) significantly ($p<0.05$). Conclusion: This study proved the modulating effect of 6-gingerol on metabolic syndrome in a dose-dependent manner through the ER stress pathway.