ANALISIS SEKRETOM hWJ-MSCs SEBAGAI HEPATOPROTEKTOR PADA SEL HepG2 YANG DIINDUKSI LIPOPOLISAKARIDA

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Diajukan untuk memenuhi sebagian syarat untuk memperoleh gelar Sarjana Sains
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PROGRAM STUDI BIOLOGI
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Dengan ini menyatakan bahwa karya tulis ini merupakan hasil kerja saya sendiri. Saya menjamin seluruh isi karya ini, baik sebagian maupun keseluruhan, bukan merupakan plagiarisme dari karya orang lain, kecuali pada bagian yang telah dinyatakan dan disebutkan sumbernya dengan jelas.

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Yang membuat pernyataan

Ismia Rahmawati

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ANALISIS SEKRETOM hWJ-MSCs SEBAGAI HEPATOPROTEKTOR PADA SEL HepG2 YANG DIINDUKSI LIPOPOLISAKARIDA

ABSTRAK

Kerusakan hati akibat inflamasi merupakan masalah kesehatan global yang memerlukan terapi inovatif dan minim efek samping. Sekretom dari human Wharton's Jelly Mesenchymal Stem Cells (hWJ-MSC)(SW) mengandung faktor bioaktif yang berpotensi sebagai agen hepatoprotektif. Penelitian ini bertujuan mengevaluasi sitotoksisitas dan aktivitas hepatoprotektif SW terhadap sel HepG2 yang diinduksi lipopolisakarida (LPS). hWJ-MSCs diisolasi dari tali pusat manusia segar. Sekretom dikoleksi dari media terkondisi hWJ-MSCs tahap 4. Pemodelan inflamasi HepG2 dilakukan dengan induksi LPS. Uji sitotoksisitas menggunakan WST-8 dilakukan pada sembilan kelompok perlakuan dan analisis ekspresi gen MMP-1 dan COL1A1 menggunakan qRT-PCR pada enam kelompok perlakuan. Hasil menunjukkan SW pada konsentrasi ≤12,5% tidak bersifat sitotoksik. Ekspresi gen COL1A1 dan MMP-1 pada kelompok perlakuan SW menurun signifikan dibanding kontrol positif ($p<0,05$) terutama pada perlakuan SW 4,17% (1,55 ± 0,29 dan 1,54 ± 0,21). Hasil ini menunjukkan bahwa SW terbukti aman dan efektif sebagai agen hepatoprotektor dengan meningkatkan viabilitas sel HepG2 yang diinduksi LPS serta secara signifikan menurunkan ekspresi gen pemicu fibrosis, yaitu COL1A1 dan MMP-1 dengan konsentrasi SW 4,17% menunjukkan hasil paling optimal.

Kata kunci: COL1A1, hepatoprotektor, HepG2, hWJ-MSCs, LPS, MMP-1, Sekretom

ANALYSIS OF SECRETOM DERIVED FROM hWJMSC AS HEPATOPROTECTOR IN LIPOPOLYSACCHARIDES-INDUCED HepG2 CELLS

ABSTRACT

Liver damage resulting from inflammation is a global health concern that requires the development of innovative therapeutic interventions with minimal adverse effects. The secretome derived from human Wharton's jelly mesenchymal stem cells (hWJ-MSCs)(SW) contains bioactive factors with the potential to act as hepatoprotective agents. This study aims to evaluate the cytotoxic and hepatoprotective activity of SW on lipopolysaccharide (LPS)-induced HepG2 cells. hWJ-MSCs were isolated from fresh human umbilical cord tissue. The secretome was collected from the conditioned medium of hWJ-MSCs at stage 4. HepG2 inflammatory modelling was performed using LPS induction. Cytotoxicity testing using WST-8 was conducted on nine treatment groups, and gene expression analysis of MMP-1 and COL1A1 was performed using qRT-PCR on six treatment groups. The results demonstrated that SW at concentrations of ≤12.5% were non-cytotoxic. Gene expression of COL1A1 and MMP-1 decreased significantly in the SW treatment groups compared to the positive control ($p < 0.05$), particularly in the 4.17% SW group (1.55 ± 0.29 and 1.54 ± 0.21). These results suggest that SW has been proven to be safe and effective as a hepatoprotective agent, as indicated by increased viability of LPS-induced HepG2 cells and a significant decrease in the expression of fibrosis-inducing genes, namely COL1A1 and MMP-1 with a concentration of 4.17% SW showing the most optimal results.

***Keywords**:COL1A1, hepatoprotector, HepG2, hWJ-MSC, MMP-1, LPS, Secretome*

DAFTAR ISI

DAFTAR TABEL

DAFTAR GAMBAR

DAFTAR LAMPIRAN

DAFTAR SINGKATAN

AFLD: *Alcoholic Fatty Liver Disease*

AMPK : *AMP-activated protein kinase*

CCK: *Cell Counting Kit 8*

COL1A1 : *Collagen type I alpha 1*

ECM: *Extracellular Matrix*

GAPDH : Glyceraldehyde-3-Phosphate Dehydrogenase

HCC: *Hepatocellular Carcinoma*

HGF: *Hepatocyte Growth Factor*

HSC: *Hepatic Stellate Cells*

hWJ-MSCs: *human Wharton's Jelly Mesenchymal Stem Cells*

IFN : Interferon

IL: Interleukin

JAK: *Janus Kinase*

KGF: *Keratinocyte Growth Factor*

LPS: *Lipopolysaccharide*

MAPK: *Mitogen-Activated Protein Kinase*

MMP: *Matrix Metalloproteinase*

MSC: *Mesenchymal Stem Cell*

MTT: 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide

NADPH: Nicotinamide Adenine Dinucleotide Phosphate

NAFLD: *Non-Alcoholic Fatty Liver Disease*

NASH: *Non-alcoholic Steatohepatitis*

PBC: *Primary Biliary Cholangitis*

PBS: *Phosphate Buffered Saline*

PCR: *Polymerase Chain Reaction*

PSC: Primary Sclerosing Cholangitis

RNA: *Ribonucleic Acid*

ROS: *Reactive Oxygen Species*

SMAD: *Suppressor of Mothers Against Decapentaplegic*

STAT: *Signal Transducer and Activator of Transcription*

SW: Sekretom *human Wharton's Jelly Mesenchymal Stem Cells*

TGF: *Transforming Growth Factor*

TIMP: *Tissue Inhibitors of Metalloproteinases*

TNF: *Tumor Necrosis Factor*

VE : Vesikel Ekstraseluler

VEGF: *Vascular Endothelial Growth Factor*

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