INTISARI

Di Indonesia, kanker ovarium memiliki prevalensi tinggi sebesar 64% dari total kasus pada tahun 2020. Upaya terus dilakukan untuk mengembangkan agen terapeutik yang menargetkan sel kanker dan bersinergi dengan sel imun dalam *Tumor Microenvironment* (TME). Salah satu antikanker potensial, senyawa kalkon 3 ($C_{15}H_{12}O$), telah terbukti menghambat pertumbuhan kanker payudara, serviks, dan kolon. Pada penelitian ini, sel kanker ovarium SKOV-3 dikokultur dengan *Peripheral Blood Mononuclear Cell* (PBMC) untuk memodelkan sel-sel imun dalam TME, sehingga perlakuan senyawa kalkon 3 dapat dilihat dari sistem monokultur SKOV-3 dan kokultur SKOV-3/PBMC. Tujuan dari penelitian ini adalah menganalisis potensi senyawa kalkon 3 sebagai antikanker dalam sistem kokultur.

Metode *in silico* dilakukan melalui *data mining* dan identifikasi protein target senyawa kalkon 3, *Protein-Protein Interaction* (PPI), analisis profil *Overall Survival* (OS) pasien kanker ovarium dan level ekspresi gen pada sel SKOV-3, serta analisis *molecular docking* senyawa kalkon 3 dengan protein target. Validasi secara *in vitro* dilakukan melalui uji sitotoksisitas dengan *MTT Assay* dan *WST-1 Assay*, deteksi apoptosis menggunakan *flowcytometer*, dan analisis ekspresi gen target menggunakan qRT-PCR.

Hasil *data mining* menunjukkan bahwa terdapat 109 gen target senyawa kalkon 3 pada kanker ovarium SKOV-3, termasuk *Epidermal Growth Factor Receptor* (*EGFR*), *Peroxisome Proliferator-Activated Receptor Gamma* (*PPARG*), *Histone Deacetylase 1* (*HDAC1*), dan *JUN* yang ekspresi tingginya menurunkan OS pasien kanker ovarium. Hasil *molecular docking* menunjukkan bahwa kalkon 3 menargetkan EGFR dan PPAR-γ dengan skor *docking* -6,5709 dan -7,1097. Hasil analisis sitotoksisitas menunjukkan bahwa kalkon 3 memiliki nilai IC_{50} sebesar 86 μM pada sistem kokultur. Hasil uji apoptosis menunjukkan bahwa pemberian senyawa kalkon 3 sebanyak 86 μM pasca kokultur meningkatkan apoptosis sebesar 54,03%. Hasil analisis ekspresi gen menunjukkan bahwa pemberian senyawa kalkon 3 pasca kokultur meningkatkan ekspresi *EGFR* dan menurunkan ekspresi *PPARG* bergantung pada dosis. Berdasarkan hasil penelitian, dapat disimpulkan bahwa senyawa kalkon 3 berpotensi sebagai antikanker ovarium dengan mentarget EGFR dan PPAR-γ.

Kata kunci : *Antikanker, kalkon 3, PBMC, SKOV-3, TME*

ABSTRACT

In Indonesia, ovarian cancer has a high prevalence of 64% of total cases in 2020. Innovation continues to be carried out to develop therapeutic agents that target cancer cells and synergize with immune cells in the *Tumor Microenvironment* (TME). One of the potential anticancer agents, chalcone 3 compound ($C_{15}H_{12}O$), has been proven to inhibit the growth of breast, cervical, and colon cancer. In this study, SKOV-3 ovarian cancer cells were co-cultured with *Peripheral Blood Mononuclear Cells* (PBMC) to model immune cells in the TME, allowing the effects of chalcone 3 to be observed from both the SKOV-3 monoculture and the SKOV-3/PBMC co-culture systems. The aim of this research is to analyze the potential of chalcone 3 as an anticancer agent in the co-culture system.

The *in silico* method was conducted through data mining and identification of target proteins of chalcone 3, *Protein-Protein Interaction* (PPI), analysis of *Overall Survival* (OS) profiles of ovarian cancer patients and gene expression levels in SKOV-3 cells, as well as molecular docking analysis of chalcone 3 with target proteins. *In vitro* validation was conducted through cytotoxicity tests using *MTT Assay* and *WST-1 Assay*, apoptosis detection using *flowcytometer*, and target gene expression analysis using qRT-PCR.

Data mining results showed that there are 109 target genes of chalcone 3 in SKOV-3 ovarian cancer, including *Epidermal Growth Factor Receptor* (*EGFR*), *Peroxisome Proliferator-Activated Receptor Gamma* (*PPARG*), *Histone Deacetylase 1* (*HDAC1*), and *JUN*, whose high expression levels decrease the OS of ovarian cancer patients. Molecular docking results show that chalcone 3 targets EGFR and PPAR-γ with docking scores of -6.5709 and -7.1097. The results of the cytotoxicity analysis show that chalcone 3 has an IC50 value of 86 μM in the co-culture system. The apoptosis test results indicate that the administration of chalcone 3 at 86 μM post-co-culture increases apoptosis by 54.03%. The gene expression analysis results show that the administration of chalcone 3 post-co-culture increases *EGFR* expression and decreases *PPARG* expression in a dose-dependent manner. Based on the research results, it can be concluded that chalcone 3 has the potential to be an ovarian anticancer agent by targeting EGFR and PPAR-γ.

Keywords : *Anticancer, chalcone 3, PBMC, SKOV-3, TME*