Studi in silico Mekanisme Antikanker N-Ters-Butil dan N-Oktil Galamida pada Sel Kanker Payudara MCF7 = In silico Study of Anticancer Mechanism of N-Tert-Butyl and N-Octyl Gallamide in MCF7 Breast Cancer Cells

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Abstrak

Asam galat dan turunannya mendapatkan perhatian khusus karena berpotensi sebagai antikanker penyakit kanker payudara. Studi pendahuluan berhasil membuktikan bahwa senyawa asam galat, N-Oktil galamida, N-Ters-Butil galamida dan N-Isoamil galamida berpotensi sebagai agen pro-apoptosis pada sel MCF7 kanker payudara. Analisis model data profil ekspresi gen sebagai respon pro-apoptosis sel kanker terhadap pemberian asam galat (GSE158788) menghasilkan sejumlah Differentially Expressed Genes (DEG) selama proses kematian sel. Hasil analisis jaringan interaksi protein – protein, pengayaan Gene Ontology (GO) dan keterkaitannya dengan jalur pensinyalan apoptosis-kanker payudara berdasarkan database Kyoto Encyclopedia of Genes and Genomes (KEGG), berhasil menyeleksi peran signifikan tertinggi dimiliki oleh gen JUN, FOS, dan MAP2K6 pada jalur pensinyalan MAPK. Uji in silico berupa simulasi molekuler dilakukan untuk mengevaluasi interaksi pengikatan antara senyawa uji sebagai inhibitor protein regulator ketiga gen, yaitu protein hulu JNK, AKT1, dan DVL. Hasil memprediksi bahwa ikatan dan kestabilan kompleks terbaik terjadi antara senyawa N-Oktil Galamida dengan protein JNK dan DVL, serta N-Ters-Butil Galamida dengan protein AKT1. Konfirmasi ekspresi gen JUN, FOS, serta produk regulasi ekspresi oleh MAP2K6, yaitu p53 serta p38, pada sel MCF7 dilakukan menggunakan metode quantitative real-time PCR. Ekspresi gen JUN dan FOS relatif mengalami peningkatan dan p38 relatif mengalami penurunan pada konsentrasi IC50.

.....Gallic acid and its derivatives receive special attention because they can act as anti-breat cancer agents. Preliminary studies have succeeded in proving that the compounds of gallic acid, N-Octyl gallamide, N-Ters-Butyl gallamide and N-Isoamyl gallamide have the potential to act as pro-apoptotic agents in breast cancer MCF7 cells. Model analysis of gene expression profile data as a pro-apoptotic response of cancer cells against administration of gallic acid (GSE158788) produced a number of Differentially Expressed Genes (DEG) during the cell death process. Protein-protein interaction network analysis, Gene Ontology (GO) enrichment and its relationship to the apoptosis-breast cancer signalling pathway based on the Kyoto Encyclopaedia of Genes and Genomes (KEGG) database, have succeeded in selecting of the JUN, FOS, and MAP2K6 genes that showed the highest significant role on the MAPK. on the MAPK signalling pathway. Molecular simulations were carried out to evaluate the binding interactions between the test compounds as inhibitors of the regulatory proteins of the three genes, namely the upstream proteins of JNK, AKT1, and DVL. The results predict that the best binding interaction and stability of the complex occurs between the N-Octyl Gallamide compound with the JNK and DVL proteins, and N-Ters-Butyl Gallamide with the AKT1 protein. Confirmation of the expression of the JUN, FOS genes, as well as the expression regulation products by MAP2K6, namely p53 and p38, in MCF7 cells was carried out using the quantitative real-time PCR method. The expression of the JUN and FOS relatively increased and p38 gene relatively decreased when treated in IC50 concentration.