POTENSI SENYAWA PENTAGAMABORONON-0-FRUKTOSA (PGB-0-F) SEBAGAI AGEN KEMOTERAPI TERHADAP SEL KANKER PAYUDARA 4T1

INTISARI

Senyawa analog kurkumin baru, Pentagamaboronon-0 (PGB-0) merupakan senyawa antikanker potensial serta dapat dikembangkan sebagai senyawa *boron carrying pharmaceutical* untuk pengobatan BNCT (*boron neuron capture therapy*). Namun senyawa tersebut memiliki kekurangan yakni kelarutan dalam air yang rendah. Tujuan penelitian ini adalah untuk mengeksplorasi aktivitas antiproliferatif dan anti-metastatik senyawa hasil kompleksasi PGB-0 dengan fruktosa, PGB-0-F terhadap sel kanker payudara 4T1. Uji sitotoksisitas dilakukan dengan metode MTT *assay* menunjukkan bahwa PGB-0-F memiliki nilai IC_{50} sebesar 33 µM pada perlakuan 24 jam sedangkan kombinasi senyawa PGB-0-F menghasilkan efek sinergis jika diberikan bersamaan dengan doxorubicin. Analisa siklus sel dengan PI-*staining flow cytometry* menunjukkan PGB-0-F memodulasi siklus sel yang menyebabkan S-*phase arrest* pada konsentrasi 34 µM dan 51 µM pada perlakuan 24 jam, yang didukung dengan adanya peubahan ekspresi *protein cyclin* A yang berperan penting pada fase S siklus sel. Selanjutnya, uji apoptosis PGB-0-F (34 dan 51 µM) menginduksi apoptosis sebesar 7,36 dan 7,18% dibandingkan kontrol sel tanpa perlakuan PGB-0-F. Uji produksi ROS intraseluler melalui perlakuan PGB-0-F 51 µM dengan DCFDA *staining* menghasilkan kenaikan ROS *level* sebesar 137% dibandingkan dengan kontrol sel. Adapun pengujian terhadap aktivitas anti-migrasi melalui metode *scratch wound healing assay*, menunjukkan PGB-0-F menghambat migrasi pada sel 4T1, sedangkan pada uji ekspresi MMP-9 dengan metode *gelatin zymography* menunjukkan adanya penurunan ekspresi protein tersebut. Berdasarkan uji anti-proliferatif dan uji anti-migrasi PGB-0-F berpotensi dikembangkan sebagai agen kemoterapi khususnya sebagai senyawa anti-migrasi.

Kata Kunci : *boron carrying pharmaceutical*, PGB-0-F, Sel 4T1, proliferasi, migrasi

POTENCY OF PENTAGAMABORONON-0-FRUCTOSE (PGB-0-F) COMPOUND AS CHEMOTERAPY AGENT TOWARD 4T1 BREAST CANCER CELLS

ABSTRACT

The new curcumin analogue compound, Pentagamaboronon-0 (PGB-0) is an potential anticancer compound which can be developed as boron carrying pharmaceutical for BNCT (boron neuron capture therapy) treatment. However, this compound has a limitation of low water solubility. The aim of this study was to explore the anti-proliferative and anti-metastatic activities of the PGB-0 complex with fructose (PGB-0-F) against 4T1 breast cancer cells. The cytotoxicity assay performed by the MTT assay method showed that PGB-0-F had an IC_{50} value of 33 μM during 24 hours treatment while the PGB-0-F combination gave a synergistic effect when administered simultaneously with doxorubicin. Analysis of cell cycle with PI staining flowcytometry showed that PGB-0-F modulated cell cycle with S-phase arrest at concentrations of 34 μM and 51 μM in 24 hour treatment, supported by expression change of cyclin A protein that plays an important role in the S phase cell cycle. Furthermore, PGB-0-F (34 and 51 μM) induced apoptosis by 7,36% and 7,18% compared to untreated cell. Intracellular ROS induction test through PGB-0-F treatment of 51 μM with DCFDA staining resulted an increase of ROS concentration of 1.4 times compared with cell control. The testing of anti-migration activity was performed by scratch wound healing assay method, showing PGB-0-F inhibited migration in 4T1 cells, whereas in MMP-9 expression experiment with gelatin zymography method showed a decrease of protein. Based on anti-proliferative tests and PGB-0-F anti-migration assays, PGB-0-F has a potency to be developed as chemotherapeutic agent especially as anti-migration agent.

Keywords : *boron carrying pharmaceutical*, PGB-0-F, 4T1 Cells, proliferation, migration