

INTISARI

Kematian akibat kanker mayoritas disebabkan oleh kegagalan dalam pencegahan metastasis. Salah satu strategi untuk dapat menarget sel kanker melalui *Boron Neutron Captured Therapy* yang menunjukkan afinitas terhadap sel-sel kanker dan dilaporkan memiliki aktivitas anti-proliferasi dan anti-metastasis terhadap sel kanker. CCRC, Fakultas Farmasi Universitas Gadjah Mada, telah mengembangkan senyawa mengandung boron bernama Pentagamaboronon-0 (PGB-0) yang diketahui memiliki aktivitas antikanker terhadap sel kanker payudara. Namun demikian, senyawa ini juga dilaporkan memiliki kekurangan terkait kelarutan yang rendah. Formulasi senyawa dengan gula sorbitol dilakukan untuk meningkatkan kelarutan dan delivery senyawa menuju sel. Tujuan dari penelitian ini adalah untuk mengetahui aktivitas anti-kanker senyawa pada sel model kanker payudara *triple negative*. Dalam penelitian ini digunakan sel model *highly metastatic* 4T1 yang digolongkan dalam sub tipe basal tanpa mengekspresikan ER, PR, maupun HER2. Uji sitotoksik dengan MTT menunjukkan senyawa PGB-0-So memiliki efek toksik semakin kuat seiring dengan peningkatan dosis (*dose-dependent manner*) dengan nilai IC_{50} 39 μ M. Dalam pengujian siklus sel dan apoptosis dengan menggunakan pewarnaan PI untuk siklus sel dan pewarnaan Annexin V-PI untuk apoptosis, diketahui perlakuan dengan senyawa PGB-0-So mampu menginduksi modulasi siklus sel untuk *arrest* fase S serta menginduksi peningkatan kematian sel melalui jalur apoptosis. Perlakuan dengan dosis sub- IC_{50} senyawa pada sel 4T1 menunjukkan potensi senyawa dalam menginduksi produksi ROS seluler yang mana peningkatan ROS diatas batas threshold mampu menginduksi terjadinya apoptosis. Disamping itu kajian terkait penghambatan aktivitas migrasi oleh senyawa dikaji melalui pengujian *scratch wound healing assay* dan uji ekspresi protein penanda metastasis *matrix metalloproteinase-9* (MMP-9) dengan *gelatin zymography*. Hasil- hasil tersebut menunjukkan bahwa senyawa PGB-0 berpotensi sebagai agen anti-kanker.

Kata Kunci: Proliferasi, Migrasi, Anti-kanker, Analog Kurkumin, PGB-0-So, Sel 4T1

ABSTRACT

Mortality in cancer is primarily due to failure of metastasis prevention. One strategy to target the cancerous cell is Boron Neutron Captured Therapy which showed high affinity toward cancer cells and reported to have anti-proliferative as well as anti-metastatic activities. CCRC, Faculty of Pharmacy Universitas Gadjah Mada, has developed boron-containing substance namely pentagama-boronon-0 (PGB-0) which is known to exhibit anticancer activity towards breast cancer cell. However it also had disadvantage regarding its low solubility. Complex formation of this substance with sorbitol was achieved to improve the delivery of this substance towards the target cells. The purposes of this research are focused to examine the anticancer activities of this compound against triple negative breast cancer cell model. In this research we used *highly metastatic* 4T1 cells which is characterized as basal subtype of breast cancer cell with no expression of ER, PR, neither does HER2. The MTT cytotoxicity assay of PGB-0-So against 4T1 breast cancer cell line were found to exert potential effect in dose-dependent manner with IC_{50} values of 39 μ M. The cytotoxicity of PGB-0-So complex was found to be increased considerably compared with that of PGB-0. Cell cycle modulation and apoptosis induction analyses on its IC_{50} , by using PI-staining and Annexin FITC-staining respectively, were found to modulate cell cycle arrest in S phase as well as induce programmed cell death, apoptosis. The sub- IC_{50} treatment of this compound was also improved the cellular reactive oxidative stress (ROS) level which also took role in apoptosis induction. In addition, the study of cell migration inhibition using gelatin zymography and *in vitro* wound healing assays on highly metastasis breast cancer cell line 4T1, following the treatment of PGB-0-So complex slightly inhibited cell migration through the repression of matrix metalloproteinase-9 (MMP-9) expression. These findings suggest that PGB-0-So is potential as an anticancer agent.

Keywords: Proliferasi, Migrasi, Anticancer, Curcumin analogue, PGB-0-So, 4T1 cell line